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GANGRENE OF THE HAND FOLLOWING TREATMENT FOR PRURITUS OF HEPATOTOXIC ORIGIN*

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THE treatment of severe pruritus is often so difficult that one is prone to seize on any remedy that seems to offer relief. Many patients enter the hospital with badly excoriated skin, traumatized by their attempts to alleviate the itching, and suffering from lack of rest and sleep. In this report we wish to describe our experiences with a patient suffering from acute hepatitis and jaundice who was given ergotamine tartrate for control of itching and who subsequently developed serious constitutional symptoms and gangrene of one hand.

A 56-year-old, married woman entered the New England Baptist Hospital on January 28, 1945, with a chief complaint of jaundice. This had been present for 2 weeks and was associated with clay-colored stools, dark urine and marked pruritus. For 2 months previously the patient had been more tired than usual, had lost 10 pounds in weight and had noticed increasing flatus and belching, with occasional vomiting. Increasing dyspnea with exertion was also present. There had been no severe pain at any time, but there had been occasional mild twinges of discomfort in the right upper quadrant of the abdomen. The past history revealed tonsillectomy 17 years previously, subtotal thyroidectomy for adenomatous goiter 15 years previously and resection of a parathyroid tumor 10 years previously.

System review was negative except for moderate deafness, dyspnea after climbing one flight of stairs, soreness in the right upper quadrant of the abdomen and occasional belching, flatus and vomiting. The menopause had begun 3½ years previously. The patient had had arthritis for several years.

Physical examination on admission showed a markedly icteric, moderately deaf woman lying restlessly in bed. There were excoriations of the skin of the abdomen and extremities, apparently caused by scratching. All the upper teeth and the lower molars were absent. Tonsillar tabs were present. There was an old thyroidectomy scar. The liver was palpable, both right and left lobes being enlarged, and there was a questionable, rather hard mass between the liver edge and the umbilicus. There were external hemorrhoidal tabs, slight pitting edema of the anterior tibia and marked dorsal kyphosis. Finally, there appeared to be slight arthritic changes of a rheumatoid nature in the fingers. The blood pressure was 140/70, the pulse 72, and the temperature 98.6°F.

The urine had a specific gravity of 1.010 and gave an acid reaction. It contained a slight trace of albumin and no sugar. The urobilinogen was demonstrable in a dilution of 1:8. The sediment contained 7 or 8 white cells per high-power field, a few bacteria and epithelial cells. It contained no bile.

The hemoglobin was 12.4 gm., and the red-cell count 3,580,000. The white-cell count was 6,650 with 68 per cent neutrophils and 32 per cent lymphocytes. The prothrombin time was 81 per cent of normal. A blood Hinton test was negative. The nonprotein nitrogen was 34 mg. per 100 cc., the total serum protein 8.9 gm., with the albumin 5.3 gm. and the globulin 3.6 gm. The serum bilirubin was 21 mg. direct. The stool was brown.

The clinical impression on admission was carcinoma of the head of the pancreas or stones in the common duct, mild congestive failure and rheumatoid arthritis. On further inquiry, it became known that the patient had received injections of cinchophen for her arthritis during 2 weeks in November, 1944, in another town. In addition, she had received sodium salicylate, iodine, colchicine, streptococcal vaccine and an unidentified stomachic.

As the laboratory work became known and the patient was further observed, the clinical impression changed to that of subacute yellow atrophy based on a toxic hepatitis, in addition to a possible obstruction of the common duct.

The patient was placed on a high-protein, high-carbohydrate, low-fat diet, along with a parenteral preparation of vitamin K and calamine lotion with 1 per cent phenol for the pruritus.

On February 3, a partial gastrointestinal series showed no intrinsic lesion in the upper tract and no widening of the duodenal loop. Daily urine urobilinogen tests were positive in dilutions varying from 1:8 to 1:16. Because of anorexia, infusions of 5 per cent glucose in water fortified with 100 mg. of thiamin chloride were given daily. Two cubic centimeters of crude liver extract was given intramuscularly every 24 hours.

On February 7, because of continued uncontrollable itching, ergotamine tartrate (Gynergen) was started in doses of 1 mg. twice daily. This produced slight to moderate relief.

Amino acids were added to the daily infusions on February 12 and were continued for 6 days. The serum bilirubin rose to 26 mg. 10 days after admission, but since the stools remained brown, the diagnosis of obstruction of the common duct was abandoned. The prognosis appeared poor, even though the serum bilirubin had declined to 12 mg. by February 13. The patient was drowsy, lethargic, anorexic and still jaundiced. The pruritus was fairly well controlled by the ergotamine tartrate.

On February 14, after 16 mg. of ergotamine had been given, it was noted that both radial pulses were weak and that numbness had developed in the right hand. On February 15, the right radial pulse could not be obtained and the numbness persisted, accompanied by aching in the right arm.

On February 17, neither radial pulse was obtainable and there was severe pain in the right hand. On this date a mottled blue-gray color first appeared on the fingers of both hands. This was intermittent and associated with some coldness of the fingers. Pulsations were present in the popliteal, posterior tibial and dorsalis pedis arteries, the feet and toes were warm, and there were no color changes in the lower extremities. Although the pain in the right hand persisted, the color changes were inconstant. Ergotamine tartrate was still being given, the total dosage having reached 26 mg. This was immediately discontinued. During the following 24 hours the extremities were unchanged, except that there was a constant dusky, pale-blue color in both hands, which were

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cold. In addition, both brachial and axillary pulsations had disappeared.

On February 21 cervical sympathetic block was done, and shortly afterward the patient thought that a little feeling had returned to the fingers of the right hand. Papaverine hydrochloride was given subcutaneously, ½ gr. every 3 hours. Buerger's exercises were started.

Although the right hand was warmer following the sympathetic block, the poor color persisted. Between February 17 and 22, the temperature gradually rose to 102°F. The left hand returned to a normal color within 36 to 48 hours following the cervical block and remained so, with only a sensation of numbness and slight stiffness in the fingers. In addition, the axillary, brachial and radial pulses returned to both arms within 48 hours after the sympathetic block and 72 hours after stopping the ergotamine tartrate.

The patient's general condition improved rapidly. By February 27 the temperature was normal and the anorexia was markedly diminished. The jaundice became less, and on March 12 the serum bilirubin was down to 2.5 mg. Papaverine was stopped on March 4.

Lines of demarcation began to form on the right hand, and it was evident that gangrene was present. By March 20, the lines between normal and gangrenous tissue were quite plain, and penicillin was started in doses of 100,000 units daily in preparation for operation. Within a few days the lines of demarcation were extremely sharp and the general appearance of all viable tissue was much improved (Fig. 1).

On March 27, the thumb and first finger of the right hand were amputated. During the operation several blood vessels were seen to be filled with old blue-black blood and the vessel walls themselves appeared to be in poor condition. The final pathological report, however, showed no evidence of specific vascular disease and only dry gangrene of the tissues.

Postoperatively the patient did satisfactorily. She was given 1½ gr. of papaverine every 3 hours by mouth, with the thought that any slight dilatation of the vessels would assist healing. This dosage was reduced to 1½ gr. every 6 hours on March 29 and the drug was stopped on April 3, when the patient experienced some anorexia and regurgitation of food, vomiting once. She was out of bed on the 2nd postoperative day and was discharged home on the 9th day, with the wound healing well. Penicillin was discontinued on the day before discharge.

A good cosmetic result was achieved, but it was expected that the function of the hand would be poor, although the stump of the thumb might prove useful. The last report from the patient stated that she was able to write with her right hand.

FIGURE 1.

It seems logical that any pharmacologic depressant of the sympathetic nervous system might give therapeutic assistance in severe pruritus, since it is held by some that an increased irritability of the sympathetic nerve endings is responsible for this condition. Following this line of reasoning, Lichtman[1] in 1931 reported 4 cases treated with ergotamine tartrate for pruritus, of renal origin in 2 cases and of hepatic origin in 2. All these patients were given 1 mg. three times a day by mouth. In each case an excellent result was obtained shortly after therapy was begun. The drug was stopped immediately on obtaining relief, and no recurrence of the pruritus was noted. Lichtman therefore recommends a dose of 1 mg. orally three times a day as a useful antipruritic in hepatic and renal disease. In addition, the drug is to be stopped as soon as relief is obtained.

In 1933, Snell and Keyes[3] reported a series of 12 cases in which ergotamine tartrate was used for relief of pruritus. They administered an oral dose of 1 mg. three or four times a day or a subcutaneous or intramuscular dose of 0.5 to 1.0 mg. daily. They concluded that the pharmacologic action of ergotamine tartrate was so little understood that it would be advisable to regard it as a purely empirical remedy. They reported no toxic effects in their cases, but considered this a possibility. The frequency with which pruritus occurs is brought out in this article, the authors mentioning that this complaint was noted in 60 per cent of patients with choledocholithiasis and in a slightly higher percentage of those with stricture of the common bile duct, especially those of long standing, and in cases in which there was extensive hepatic injury. In neoplastic obstruction itching was encountered in at least 75 per cent of cases.

In 1936, Yater and Cahill[5] reported a case treated for severe pruritus by 0.5 mg. of ergotamine tartrate three times a day by injection. This was given for six and a third days, the total dosage being 9.5 mg. On the second day coldness of the arms occurred as a premonitory symptom of toxicity, and as a final result it was necessary to amputate both legs halfway between the knee and the foot. No permanent injury to the upper extremities occurred. Microscopic examination showed that all the arteries were constricted to varying degrees and often thrombosed in the less constricted regions. The authors described the two forms of ergotism, the convulsive and gangrenous types.

In the same year, Gould, Price and Ginsburg[4] described a case in which the patient was thought to be suffering from toxic liver damage, secondary to neoarsphenamine. Because of pruritus, 0.25 mg. of ergotamine tartrate was given subcutaneously daily for four days. Following the second injection, pain and coldness developed in the extremities, soon followed by cyanosis and impaired sensation. Both hands also became cold and cyanotic, the dorsalis pedis and tibial arteries could not be felt and the pulsation in the popliteal artery was barely palpable. Ergotamine tartrate was discontinued and the patient was given vasodilators (glyceryl trinitrate and amyl nitrite), as well as strychnine sulfate. Progressive involvement of the legs occurred until there was blackness of the lower two thirds, complicated by skin macerations. There was definite narrowing of the fundal arteries. The patient became worse and died four days after the initial dose of ergotamine tartrate. Post-mortem examination showed all the arterioles examined to be contracted.

In 1939, Comfort and Erickson[6] presented an excellent review of the untoward effects following the use of ergot and ergotamine tartrate. They also believed that there was no clear, rational explanation for the occasional marked relief noted in cases of pruritus following the use of ergotamine. A brief review of the literature concerning untoward effects from the use of ergot and ergotamine tartrate was given. They divided this review into groups according to the condition for which ergotamine was given; these groups included puerperal sepsis, menorrhagia, hyperthyroidism, jaundice and pruritus. Following this review, Comfort and Erickson presented 2 cases treated at the Mayo Clinic with ergotamine tartrate in which untoward effects developed. In the first case the drug in oral doses of 1 mg. three times a day was given for pruritus, apparently due to stricture of the common duct. A total of 23 mg. was given. Following this there developed coldness of all extremities, cyanosis of the right hand and wrist and inability to move the fingers of the right hand. Pulsations could not be felt in the left ulnar or the right radial and ulnar arteries, and could be felt only slightly in the left radial artery. Continuous hot moist packs were applied, and ephedrine was given. In addition to this, alcohol was given by mouth every four hours. On this regime the extremities gradually improved. The final result in this case showed some residual muscular atrophy in the right hand. The second case was diagnosed as metastatic carcinoma of the liver. Pruritus was controlled by one to three tablets of ergotamine tartrate daily. Eight days following admission to the hospital, the radial pulse could be palpated only with the greatest difficulty, and ergotamine tartrate, of which 16 mg. had been given, was discontinued. On the next day the pulses were more easily palpable, and the following day they had returned to their normal volume. These authors concluded that some of the untoward effects from the use of one of the preparations of ergot or ergotamine tartrate recorded in the literature have followed the administration of doses larger than those compatible with good practice. In other cases, however, the bad effects have apparently been dependent on the existence of an individual idiosyncrasy to the drug, since extremely small doses have occasionally produced toxic results. In spite of the many reported cases of ergotism, the authors concluded that the value of ergotamine tartrate in doses of proper size, provided adequate precautions are taken, was such that they would continue to use the medication, especially in the control of pruritus and migraine. They emphasized the contraindications to its use and the danger of the development of ergotism, and pointed out that the onset of this complication may be suspected early by frequent examination of the arterial pulsations and of the extremities for spasm and by recognition of its early symptoms. For treatment they recommended pilocarpine subcutaneously, magnesium sulfate parenterally and alcohol orally.

In 1938, von Storch[6] thoroughly reviewed the literature concerning ill effects following the use of ergotamine tartrate. At that time it was said that the great majority of such effects occurred because

of overdosage, pre-existing sepsis or obliterative vascular disease. No serious effects were reported in the author's experience in treating migraine headaches with this drug for the previous five years. He concluded that, although migraine headaches may apparently be treated with considerable success by the use of carefully controlled doses of ergotamine tartrate, its use in the treatment of pruritus is fraught with considerable hazard.

Several experimental studies have been reported in an attempt to clarify the pharmacologic and toxic effects following the administration of ergotamine tartrate. In 1935, McGrath[7] reported on experimental ergotism produced in the tails of rats treated with ergotamine tartrate. The lesions were quite similar to that of thromboangiitis obliterans, with marked cellular proliferation and swelling in the intima, most strikingly seen in the arterioles and small arteries. Administration of theelin protected the rats from pathologic changes, and McGrath concluded that the failure of thromboangiitis obliterans to develop in the female was probably due to protection from estrogenic substances.

In 1938, however, Loewe and Lenke[8] found that theelin and Progynon B were ineffective in preventing the development of gangrene in white rats, even when treatment was begun on the day that ergotrate was first given.

From the previously described cases and others,[9–25] it becomes apparent that a considerable number of cases of peripheral gangrene have occurred following the use of ergot or ergotamine tartrate preparations. The most important toxic disturbances due to ergotamine tartrate besides gangrene are headache, nausea, vomiting, diarrhea and dizziness. Less frequently observed are weakness, itching, coldness of the skin, thirst, drowsiness, cyanosis, collapse, anginal pain, tachycardia, or bradycardia, muscular twitching or cramps, convulsions, hepatic symptoms and sudden death.

Contraindications to the use of ergotamine tartrate are well summarized by von Storch[6] as a septic state, cardiovascular disease and obliterative vascular disease. Treatment should be used with caution in cases of arteriosclerosis, hepatic or renal disease and hypersensitivity to the drug. It is certainly most strongly to be recommended that careful daily palpations of the radial and ulnar arteries, along with those of the posterior tibial, popliteal and dorsalis pedis arteries, be carried out in all cases in which ergotamine tartrate is being used for the control of pruritus. The patient should also be carefully questioned for any symptoms of numbness, tingling, coldness or pain in the extremities. Should any of these symptoms or signs be noted, the drug should immediately be stopped and measures taken to promote peripheral circulation. These measures include the intravenous use of papaverine hydrochloride and the oral use of ephedrine, papaverine hydrochloride and alcohol. Magnesium sulfate intravenously or 1 per cent pilocarpine subcutaneously may be helpful. Roch[23] has suggested acetylcholine. In this condition, however, by far the most effective treatment is prophylaxis, which consists of the immediate cessation of ergotamine tartrate therapy when any of the previously mentioned signs are noted. It cannot be too strongly stressed that most careful daily observation of the patient by the physician in charge is essential for the safe administration of this medicine. The physician who is driven to its use for the control of intractable pruritus should be well aware of its dangers and be prepared to take immediate steps to counteract them.

Conclusions

In treating severe pruritus one should be careful in the choice of a therapeutic agent, with regard to the possible toxic effects. The worse is the general systemic condition of the patient, the greater is the danger of toxicity from drugs used to control pruritus.

Ergotamine tartrate is definitely useful as an antipruritic agent provided one realizes the potentialities for severe reaction in its use.

If ergotamine tartrate is to be used as an antipruritic, the following precautions seem indicated. The dose should not exceed 1 mg. three times a day orally. At least once daily, and preferably twice, the patient should be questioned and examined concerning pain, coldness, cyanosis, loss of arterial pulsations, impaired sensation and tingling in the extremities. Should any of these signs or symptoms develop, the drug should immediately be discontinued and appropriate therapy started.

Therapy for ergot poisoning following the use of ergotamine tartrate includes the following: papaverine hydrochloride (0.02–0.03 gm.) intravenously or orally or both; ephedrine (24 mg.) orally; alcohol (15 cc. every four hours) orally; magnesium sulfate (15-20 cc. of a 3 per cent solution intravenously); 1 per cent pilocarpine (1 cc. subcutaneously); acetylcholine; and sympathetic block with novocain.

The use of ergotamine tartrate is contraindicated in the presence of a septic state, cardiovascular disease and obliterative vascular disease. It should be employed with great caution in cases of hepatic or renal disease, arteriosclerosis and hypersensitivity to the drug.

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THE DICK TEST IN MILITARY PERSONNEL*

With Special Reference to the Pathogenesis of the Skin Reaction

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THE Dick skin test has been widely used for the detection of human beings susceptible to scarlet fever and has proved to be useful for this purpose. It has been demonstrated that a skin rash rarely appears in any but Dick-positive patients during an infection by a scarlatinogenic strain of hemolytic streptococcus. There is no evidence that failure to react to the erythrogenic toxin confers protection against infection by hemolytic streptococci. In fact, recent investigation shows that cases of respiratory infection associated with skin rash caused by these organisms occur much less frequently than do those without a rash, because a large number of highly invasive strains of streptococci are apparently unable to form the skin-reacting substance.

It has usually been believed that the reaction following the injection of culture filtrates of the hemolytic streptococcus in the Dick test is due to the direct toxic action of the products of the organism on the skin.[1] The inhibition of this reaction by the preinjection incubation of the toxin with immune serum, or in vivo in the insusceptible human being, may then be regarded as an ordinary toxin-antitoxin neutralization. Others have suggested that the phenomenon is the result of hypersensitivity of the allergic type.[2]

The frequency of occurrence of positive Dick reactions has been repeatedly determined in relation to age[3] and geographical distribution.[4–10] Recently an opportunity arose to investigate the effect of certain geographical and environmental factors on the incidence of positive and negative Dick reactions in a large group of military personnel. The information obtained is presented because a similar group does not appear to have been previously studied in the United States, and because the results permit a reinterpretation of the pathogenesis of the Dick reaction.

Methods

The skin test was performed exactly as described by the Dicks.[1] All needles and syringes were boiled in distilled water and rinsed with toxin before use. A skin-test dose of toxin (Lederle) contained in 0.1 cc. of solution was injected intracutaneously in the flexor surface of the forearm. The test was read twenty to twenty-four hours later and was regarded as positive if the diameter of the area of erythema was greater than 1 cm.

A possible source of error has been introduced by the failure to perform control tests with heated toxin for the purpose of excluding so-called "pseudo-reactions." The Dicks and many others have con-

*This work was done during a field study by the Commission on Hemolytic Streptococcal Infections, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, United States Army. The Laboratories of the Department of Medicine, Stanford University School of Medicine, San Francisco, California, were made available to the commission for certain purposes.

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sidered this precaution to be unnecessary with suitably prepared testing materials. The observed positive reactions appeared to be of the correct type and were reversed during convalescence from scarlet fever in the expected manner.

Results

The reaction to Dick toxin of 1280 white men suffering from acute respiratory disease admitted to a large station hospital was determined on the second hospital day. There was no discrimination, all cases during the study period being included. The test was positive in 27.8 per cent. Three hundred and ninety-seven of these men were believed, on clinical and bacteriologic grounds, to suffer from Group A hemolytic streptococcus sore throat. Twenty-four developed a typical scarlatinaform rash. A significant antistreptolysin or antifibrinolysin response or both was observed in 87.9 per cent of 342 of these patients in whom suitable tests were done, indicating that the clinical impression was usually correct. The Dick test was positive in 27.7 per cent of this group. The relation of the results of this test to the clinical course of hemolytic streptococcus respiratory disease will be presented elsewhere.

The disease was clinically compatible with a virus type of infection in 803 cases, and no Group A hemolytic streptococci were isolated from the nasopharynx. Of these men, 27.2 per cent were Dick positive. In another 80 patients the diagnosis was not clearly established on clinical and bacteriologic grounds. These infections appeared to be examples of virus-type respiratory disease occurring in persons who were nasopharyngeal carriers of Group A hemolytic streptococci. An antibody response was demonstrated in only 2 of 18 cases studied in this group. Thirty-five per cent of these patients were Dick positive.

Age

The relation of age to positive Dick reactions is presented in Table 1. Men over the age of twenty react to Dick toxin in less numbers than do younger men. The groups are large and the results are of statistical significance. A precise analysis was not made, but it is logical to assume that men in the older age groups frequently had had a more prolonged military service, which, as will be demonstrated, decreases the incidence of positive Dick reactions.

Table 1. *Relation of Age to Dick Positivity.*

Age	No. of Men Studied	Dick Positive	
		No.	Percentage
yr.			
17 to 20	407	143	35.1
21 to 24	397	92	23.1
25 to 30	290	64	22.1
31 to 35	128	35	27.3
36 and over	49	15	30.6

Duration of Military Service

When the study group was considered in relation to the duration of military service, it was discovered that the incidence of Dick positivity was high (34.3 per cent) in men who had been in the Army for less than a year and fell abruptly to much lower levels (22.0 per cent) among all those who had served for a longer period of time. No significant difference existed in the rate of six-month periods of service from thirteen to more than thirty-six months. The essential data are presented in Table 2.

Duration of Service in Study Post

This survey was conducted in an Army camp located in an area in which hemolytic streptococcus disease was exceedingly frequent. Approximately one third of all cases of respiratory infection admitted to the station hospital were caused by this organism. It was of interest to ascertain whether prolonged service in this post could be demonstrated to modify the incidence of Dick positivity. The essential data are presented in Table 3. No significant alteration in the frequency of positive Dick reaction occurred after men had served in the study post for twelve months. Consideration of the effect of more than one year of residence was impossible because insufficient personnel had been stationed there for a longer period of time.

Table 2. *Relation of Military Service to Dick Positivity.*

Duration of Service	No. of Men Studied	Dick Positive	
		No.	Percentage
mo.			
0 to 6	181	62	34.3
7 to 12	429	147	34.3
13 to 18	306	73	20.3
19 to 24	118	30	28.1
25 to 36	121	22	18.9
36 and over	125	22	18.0

Table 3. *Relation of Duration of Service at Study Post to Dick Positivity.*

Duration of Service at Study Post	No. of Men Studied	Dick Positive	
		No.	Percentage
mo.			
Less than 1	705	202	28.6
1 to 6	277	67	24.2
7 to 12	232	69	29.7
13 and over	61	18	29.5

Premilitary Residence

The premilitary residence of all the tested men by states was ascertained, and the frequency of

positive Dick reactions in relation to this factor was determined. The data, classified by geographical regions, are presented in Table 4. The incidence of positive Dick reactions was extremely high (38.8 to 41.3 per cent) among those who had lived in New England, New York or the Far West; it was lower (20.0 to 33.3 per cent) among those from the remainder of the North, Middle West and West, and extremely low (8.7 to 14.0 per cent) in the border states, the Southeast and the Southwest. These differences are very great and of unquestionable statistical significance. As an added check, the duration of military service and age of men in the low-incidence areas were studied and discovered to approximate the distribution of these factors in the group as a whole.

TABLE 4. *Relation of Preliminary Residence to Dick Positivity.*

AREA*	No. of Men Studied	Dick Positive	
		NO.	PERCENTAGE
1	127	50	39.3
2	152	59	38.8
3	121	32	26.5
4	80	16	20.0
5	100	14	14.0
6	114	11	9.6
7	103	9	8.7
8	267	84	31.4
9	90	30	33.3
10	34	10	29.4
11	92	38	41.3

*The areas are as follows: 1 — New England: Maine, New Hampshire, Vermont, Massachusetts, Connecticut and Rhode Island; 2 — New York; 3 — North Atlantic states: Pennsylvania, New Jersey, Delaware and Maryland; 4 — Middle Atlantic states: Virginia, North Carolina and South Carolina; 5 — border states: West Virginia, Kentucky, Tennessee; 6 — South East: Georgia, Florida, Alabama, Mississippi, Louisiana and Arkansas; 7 — South West: Texas, Oklahoma, Arizona and New Mexico; 8 — Great Lakes states: Ohio, Indiana, Illinois, Michigan, Wisconsin, and Minnesota; 9 — Middle West: North Dakota, South Dakota, Nebraska, Kansas, Iowa and Missouri; 10 — Rocky Mountain states: Montana, Idaho, Wyoming, Colorado and Utah; 11 — Far West: California, Washington and Oregon.

Discussion

Certain information obtained during this study is of general interest. Slightly more than 25 per cent of white American men of military age were Dick positive. The frequency was increased below and decreased above the age of twenty, but the differences were not great. These facts are in accord with previous investigations in the United States.

The incidence of positive Dick reactions was the same in men admitted to the hospital with virus-type respiratory disease as in those with Group A hemolytic streptococcus sore throat, demonstrating that there is no relation between the Dick reaction and immunity to infection by hemolytic streptococci. This fact has been previously established[11] but has been insufficiently emphasized.

It is also worth while to record the information that men become less frequently Dick positive with prolonged military service. This effect did not become manifest before the end of the twelfth month. As much as one year of service in the study post, which was located in an area of extremely high incidence of hemolytic streptococcus respiratory disease, was not followed by an increase in the frequency of negative Dick reactions.

The most interesting information obtained during this study was that which appeared to be useful in the interpretation of the pathogenesis of the Dick reaction. The originators of this test proposed the theory that the erythema was due to the direct toxic action of the skin of a filterable product of the hemolytic streptococcus and that a negative reaction would result from the presence of an antitoxin in the blood and tissues.[1] The latter substance would be acquired either by transplacental transfer of antibody in the infant or by streptococcal infection in later life. This theory of the mechanism is supported by the fact that immune human or animal serum neutralizes the toxin in vitro and that the administration of antitoxin locally or generally blanches the rash in scarlet fever.

Although this theory of the pathogenesis of the Dick reaction has been widely accepted, it is not in accord with most of the studies that have been made for the purpose of elucidating it. Most important is the established fact that infants are Dick negative regardless of the reaction of the mother or the presence or absence of antitoxin in her or in the infant's serum.[12–14] Most of these babies later become Dick positive, but do so at irregular intervals. Children of various ages who have been tested over considerable intervals of time have been observed frequently to acquire but rarely to lose the ability to react to the erythrogenic toxin.[15, 16] Maternal antitoxin transferred through the placenta should disappear promptly in children, and all subjects capable of becoming Dick positive should have done so by the end of the first year of life. More elaborate experiments have demonstrated that it is possible to transfer passively Dick positivity to Dick-negative subjects by the transfusion of serum.[17] In addition, it has been pointed out that the streptococcal erythrogenic toxin is much more heat stable than the other well known bacterial toxins.

All these facts, and others not described, have been correlated in an interpretation that states that the ability to react to Dick toxin is not a natural characteristic of human beings but is acquired as the result of exposure to the hemolytic streptococcus, and that it is a hypersensitivity phenomenon of the allergic type.[2]

A comparison of the geographical incidence of positive Dick reactions and of hemolytic streptococcus sore throat might permit a decision which of the two mechanisms described above is correct. If the ability to react to Dick toxin is a natural characteristic that may be lost by exposure to hemolytic streptococci and the subsequent development of immunity following clinical and inapparent infection, the incidence of positive reactors should be low in areas where streptococcal disease occurs frequently and high in those in which this disease is

rare. On the other hand, if a positive Dick reaction is the result of hypersensitivity acquired by exposure to the hemolytic streptococcus, the exact reverse should occur.

When the data on the geographical distribution of Dick positivity obtained during this study are considered, it is discovered that the latter situation prevails. It is difficult to state accurately the frequency of hemolytic streptococcus respiratory infection throughout the United States, but extensive studies of acute respiratory disease in military personnel and inspection of the distribution of cases of scarlet fever and rheumatic fever in the armed forces and in the civilian population indicate that the hemolytic streptococcus is rarely the cause of respiratory disease in the southern states.[18–22] Elsewhere this organism is known to be responsible for a large but unknown percentage of infections of the respiratory tract. It seems quite certain, therefore, that men whose premilitary residence has been in an area in which streptococcal disease occurs infrequently are rarely Dick positive.

An examination of published studies reveals that this fact has been previously established. A careful study in Rio de Janeiro[5, 6] showed that scarlet fever was extremely infrequent and that Dick-positive persons were rare in all age groups. Many other investigations[4–10] have confirmed the fact that positive Dick reactions are infrequent in the Tropics and in isolated Arctic communities where streptococcal disease is usually believed to be infrequent.[23] The fact that these surveys were carried out in a variety of racial groups in areas in which the incidence of streptococcal disease had been poorly assessed detracts from their usefulness.

The frequency of positive Dick reactions in a large number of Chinese students from all sections of the country was determined by Lai.[7] Those who had lived in northern China, where scarlet fever is widespread and severe, showed a frequency of positive reactions three times that of those whose residence had been in the tropical provinces, where the disease is rare.

It may be said to be established that the incidence of positive Dick reactions is low in the parts of the world in which infection by hemolytic streptococci is an infrequent occurrence. The possibility that this is due to racial variations is eliminated by the study of homogeneous population groups in China and in the United States.

Previous workers have believed that this phenomenon is to be explained on the basis of a high natural immunity to the streptococcus toxin, although at least one observer failed to find circulating antitoxin in the serum of Dick-negative persons in the Tropics.[8]

The present study strongly suggests that a hypothesis based on natural immunity is in error, since there appears to be no reason to suppose that white residents of the southern United States should have natural antibodies differing from those present in persons living in the North.

Since Dick positivity and hemolytic streptococcus infection occur infrequently in certain areas, and the reverse is true, the inescapable conclusion is that contact with the streptococcus is essential for the establishment of skin reactivity to the erythrogenic toxin. If this is the case, it is impossible to regard this material as a true toxin, and the skin reaction must be regarded as a hypersensitivity phenomenon. It is recognized that this skin reaction is somewhat different from others of an allergic nature, since it may be readily reversed during convalescence from scarlet fever or by active immunization. That this may be due to desensitization rather than to true toxin-antitoxin neutralization has been suggested.[2]

If the conclusion is acceptable that exposure to streptococcal infection is necessary for the establishment of a positive Dick reaction, the frequency of positive reactors in a population may be used as a rough guide to the incidence of streptococcal infection in the group. The occurrence of nonscarlatinogenic strains of Group A streptococci suggests an important source of error in such a procedure, since many examples of streptococcal disease occur in certain populations as the result of infection by such streptococci but sensitization of the affected persons may not result.

Summary

The reaction to Dick toxin of 1280 white men of military age was studied.

The frequency of positive reactions was least in men over the age of twenty and in those who had had more than twelve months of military service.

Positive Dick reactions were infrequent in men whose premilitary residence had been in a geographical area in which the incidence of hemolytic streptococcus disease is known to be low.

It is concluded that exposure to the hemolytic streptococcus is essential for the establishment of a positive Dick reaction.

The Dick reaction is probably the result of acquired hypersensitivity to the products of the streptococcus rather than of a natural susceptibility to a true toxin.

We are indebted to Miss Elizabeth Randall, who performed all the skin tests, and to Mrs. Helen Rantz, who compiled the data.

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PRIMITIVE MEDICINE*

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ANY discussion of so-called "primitive medicine" must begin with an essential clarification. When one speaks of primitive medicine, one refers to a special body of traditional knowledge which compared with that of the present appears crude and undeveloped. It is desirable to remember that this lack of development is a function not of the group's biologic status but of its cultural status, and that its cultural status is, again, a function not of its biologic makeup but primarily of the history of its experience as a social group.

The comparatively undeveloped medical knowledge and practice of isolated man is simply a reflection of the fact that such a person has not experienced the kind of culturalizing conditions that have fallen to the lot of man living in the Western world. The former has not developed so complex a culture as has Western man, for the reason that he has been completely isolated from the main stream and cross currents of cultural interchange and development to which man in the Western world has been exposed. Any reference to the medicine or culture of isolated man — a phrase in many ways to be preferred to the usual "primitive man" — in terms of inferiority to our superior selves is to be deprecated. To compare the cultural achievements of any two groups for the purpose of valuation, it is first necessary to determine whether they have had the same or similar opportunities for cultural achievement.

Compared with the history of experience and opportunity that Western man has enjoyed, that of isolated man has been of the most minimal kind. This fact should sufficiently account for the cultural differences that one observes, as a whole, to exist between them, and it should explain the comparative lack of complexity that characterizes the medical knowledge of isolated man.

However ridiculous and stupid some of the medical beliefs and practices may appear to the sophisticated Westerner, it should be enough here to say that this attitude is but a confession of ignorance and a lack of a historical sense and something of human understanding, for the medical lore of isolated man represents a perfectly harmonious part of the acquired wisdom of the group and a thoroughly integrated part of the social structure as a whole. Occurring in the culture in which it does, it could hardly be other than it is.

The time has long since passed when the medical lore, the leechcraft, of isolated peoples could be classed with the quaint and queer in the album of medical curiosities. Nor is it sufficient to record the bare details of that lore, as is almost invariably done in present-day histories of medicine. Medicine is a social phenomenon, and the medicine of any people can only be effectively understood as such. For this reason it is necessary to gain an understanding of the society as a whole if its medical knowledge and practice are to be understood in their full significance — if, indeed, that knowledge and practice are to be understood at all. This is particularly the case in isolated societies, in which medicine is much more closely integrated with the institutions and beliefs of the society as a whole than it is in the highly diversified structures of Western societies. Failure to recognize these elementary facts makes the chapters on primitive medicine in contemporary histories of medicine their least satisfactory ones.

Special studies of the medicine of several primitive peoples that have been written by physicians with anthropologic training are now available, and there is a vast amount of material to be found in the field studies of anthropologists.[1-14] There is a serious need of additional special field studies of the medicine of particular primitive peoples, but until these have been carried out, a highly desirable step

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would be a stocktaking of what is already known and an attempt at an analysis and systematization of this at present widely scattered knowledge. The attempt would be an extremely rewarding undertaking, and it is one that merits the attention of the serious student.

At this point I should like to discuss briefly the time-honored and perennial error that seems to have established itself in the minds of many writers on the subject — namely, the idea that both medicine and science grew out of magic. Magic may be defined as the process of manipulating the supernatural, of coercing or procuring it to do one's bidding by the performance of certain ritual acts. Science may be defined as verifiable and communicable knowledge, based on observation, experiment and reflection — in short, on doing one's utmost with one's mind, as Percy Bridgman has so fittingly put it. Now, magic and science both deal with causation, — magic with supernatural causation and science with natural causation, — and the reliance that people put on these two ways of manipulating the world in which they live is well-nigh universal. Both magic and science are mechanical procedures, but whereas the purpose of the former is the compulsion of the supernatural according to letter-perfect traditional rules of thumb, the latter has no place whatever for the supernatural, which is the main concern of magic. Science deals with cause-and-effect sequences in the natural world — experimentally gauged and determined. Magical cause and effect represent nothing but fabrications of the human mind operating in an imaginary world — the supernatural. Magic is based on a series of false analogies, whereas science is based on a rigorous testing and verification of repeatable experiences.

Every people defines the natural and the supernatural in its own way, but there is general agreement on the essential principles involved. It is only in certain sophisticated areas of Western society that some men have definitely discarded the picture of the universe as operating on two parallel and contrasted sets of causation. Primitive peoples recognize ordinary natural sequences of cause and effect, just as they also recognize more wonderful causations, — the supernatural, — technics that are not checked against natural laws but are solely concerned with manipulating a special potency that has its own rules apart from the matter-of-fact ones of craft and industry.

To manipulate the natural world man everywhere develops a material technology. No living or extinct people of whom there is any knowledge is ignorant of technologic facts. The very process of getting a living, even at the simplest imaginable levels, demands the development of certain technologic processes for manipulating the environment. The material culture of isolated peoples everywhere abundantly testifies to their ingenuity, inventiveness and technologic proficiency.

It should be fairly clear that where material technology is present, — and it is present in all human societies, — it becomes quite unnecessary to derive science from anything other than the development and practice of the technics involved and the reflecting and philosophizing on them in which man everywhere is wont to indulge.* A simple diagram will illustrate the actual relations. To manipulate the natural world man develops a material technology, and it is out of this that science eventually grows. To manipulate the supernatural world he develops a series of magical technics. There is no necessary association between the one and the other.

Natural World	Supernatural
Technology	Magic
Science	

Close study of the conditions actually prevailing in isolated societies reveals the fact that magical and scientific activities are frequently pursued as parallel activities quite independently of each other. For example, to restrict the discussion to the medical referent, when a limb is broken it is set in accordance with the best available empirical knowledge that the native doctor as a highly specialized member of the tribe has been able to obtain. No magic or ritual is involved in the treatment of the injured limb. When a person has suffered from severe and prolonged headache his skull may be trephined, and if he does not get better it is trephined until he does — or dies. No magic is involved in this either. In short, isolated peoples have their rational medicine, which is based entirely on experience and into which no element of the magical enters. Experience has taught them that certain plants possess specific qualities of medicinal value; they are therefore rationally used, and so it is with many other facts and practices that have been acquired and developed through experience. Isolated peoples also have their magical medicine, in which the principal reliance is placed on the compulsion of the supernatural. All this is not to say that magical medicine and rational medicine or science are always unrelated, for the fact is that they are frequently related, and it is often quite difficult to disentangle them. This is, however, to say that persons who are members of isolated societies are by no means fools, and that they do not live under the unrelieved domination of a host of magical ideas and practices. Nor are they, as some writers have suggested, characterized by a prelogical type of thought. If anything they suffer from an excess of logic rather than from a deficiency of it. It is an interesting fact that such

*For primitive man as a philosopher see Paul Radin.[15] On the strictly scientific accomplishments of isolated peoples Professor Wilson Wallis, of the University of Minnesota, has gathered together a vast amount of material. This work is about to be published.

drugs as quinine, curare, opium and digitalis, to name but a few, were all discovered by isolated peoples as specifics for certain conditions, and that in such practical phases of medicine as surgery many serious operations have, from earliest times, been performed on human beings with complete success. Fractures of every sort have been repaired, dislocations corrected, and obstructions removed.

This paper will attempt a brief inquiry into the types of disease concepts that are to be found in the cultures of isolated peoples, and their classification, so that they may be efficiently compared and articulated with those of the technologically more advanced Western world.

As a basis for comparing the medical concepts and practices of isolated peoples with those prevailing among the peoples of Western societies, three causes may be recognized that are universally known to explain disease. The first is natural cause, the second is human agency, and the third is supernatural agency. If the disease can be explained in terms of material agencies, it is attributed to natural causes, but if it is attributable to the action of some human being who has, for example, resorted to sorcery, the malady is assigned to a human agency. Finally, if the illness is held to be due to some spiritual or supernatural being or principle, it is ascribed to the direct action of the supernatural.

The three possible causes of disease here stated are those that, among sophisticated and isolated peoples alike, are accepted the world over. The principal difference between the concepts held by peoples with widely differing cultures is that groups with greater educational advantages—in the Western sense of those words — tend to place more confidence in the natural causation of disease, whereas isolated peoples tend to place more confidence in its supernatural causes. As everyone is aware, even in our own society there are really very few persons who do not retain some belief in the supernatural causation of disease; nor is it necessary to point out that the less educated a person is, the likelier he is to place his faith in the supernatural explanation of disease. In many parts of Europe there exist at the present time populations who believe quite as much in the supernatural causation of disease as do the most isolated peoples.*

When a man can come more or less closely to discerning the empirical elements in a situation, his reasoning is likely to be logical and based on common sense. On the other hand, when the situation with which he is concerned defies such definition, he tends to accept explanations that are no more explicitly denotable than are the conditions with which he is dealing.†

In most isolated societies it is a firm tenet of belief that the world is animated by some spiritual principle or power. This, in fact, is the definition of the supernatural — namely, the belief in the unseen, mysterious and wonderful spiritual force or powers that pervade the universe. The supernatural is generally personified in the form of a being or several beings, each with particular powers that greatly transcend anything of which man alone is capable. This belief is called "animism" by anthropologists. The power of the supernatural may also manifest itself in a disembodied form, as a supernatural quality or an attribute of objects, just as color, weight and hardness are attributes of objects. Examples are the "orenda" of the Iroquois, the Algonquian "manitou" and the Melanesian "mana." This form of the belief in the power of the supernatural is known as animatism.‡

In passing it may be noted that primitive religion may be regarded as the technic and result of supernaturalism. Religion differs from magic in that it makes no attempt to coerce but is directed toward entering into closer personal relations with the supernatural; one prays, beseeches or worships, but one never controls.§

In animistic societies it is, of course, a simple matter to explain almost everything of unknown causation as due to the activity of good or evil spirits. Magic consists of compelling these spirits to do one's bidding. Their manipulation for evil purposes is sometimes called "black magic," whereas their manipulation for good purposes is called "white magic." The practice of magic in any form is called "sorcery."

At the very outset one sees how intimately related to the character of a culture are the concepts of disease that it holds, for it is obvious that in a sophisticated society in which the experimental method occupies a prominent place, the doctrine of natural causes will be the one most generally accepted as an explanation of disease. Where the habit of thought associated with the experimental method is wanting and spiritistic beliefs are the dominant ones, the tendency will be to explain disease in terms of the supernatural.

Classification of Disease Concepts

Given the cultural character of a typical isolated society, there may be recognized seven main types of primitive disease concepts. These are as follows: sorcery or magic, breach of taboo, disease-object intrusion, spirit intrusion, soul or body loss, dreaming and independent occurrence.

*For an admirable study of the folk medicine of a European peasantry, — of the Balkans, in this instance, — see Kemp[10] and Brendle and Unger.[11]

†Any object to which the human organism can react serially point for point may be referred to as "explicitly denotable." The objects known as "finger" or "penny" or "stone" belong to this class. Such entities as "Fascism," "democracy" and "nation," to which a person cannot react in this way, are denoted by terms referable to "implicit language usage." [17]

‡There is serious question whether the distinction between animism and animatism can be legitimately maintained, since in the final analysis the supernatural attributes of an object may be traced back to some definitely recognized personified spiritual agency. For an excellent discussion of this matter see Karsten.[18]

§In the discussion of these matters it is well to remember that there are no attitudes toward supernatural relations that are not taken toward human relations. Honor and awe are not given to human beings to the extent to which they are shown toward the supernatural beings, the gods; the only difference is one of extent.

Sorcery or Magic

When it is believed that disease is produced by the activities of persons skilled in magic or by the manipulations of older persons who exercise some control over the supernatural, the disease is said to be produced by sorcery or magic. In isolated societies there are generally available a number of magical ritual formulas that can be enacted by anyone to compel the supernatural to produce disease and even death in some other person, whether of one's own or another tribe. In addition there is always present a special class of persons, the medicine men, who are particularly skillful in manipulating the supernatural for good or evil. These may be hired at almost any time to bring affliction to one's enemies.

The magic by which these conditions are produced is of two kinds, homeopathic or imitative magic and contagious magic. Homeopathic magic assumes that things that resemble each other are the same. An image, for example, is made of one's enemy and this is injured or destroyed, in the belief that the victim will thereby be injured or destroyed.

Contagious magic makes the assumption that things that have once been in contact are always in contact; therefore, whatever is done to the one must similarly affect the other. According to this view, a person is never really dissociated from any part of his body or anything that has been in contact with it. Thus, his nail parings, hair, spittle and clothing are all part of him, so that anyone who obtains possession of these can, at any distance, work his will on the person of whom they were once a part.

In practice both homeopathic and contagious magic are often combined; more exactly, whereas homeopathic magic may be practiced by itself, contagious magic will generally be found to involve an application of the homeopathic principle. Both branches of magic are comprehended under the general name of "sympathetic magic," since both assume that things act on each other at a distance through a connecting invisible ether.

Under such conditions of belief, causation of disease by sorcery is brought in to explain not only illnesses that have no obvious antecedent cause but also those in which the natural cause is obvious. For example, when a man stumbles and bruises himself or falls from a tree and injures himself, the cause is not ascribed to the boulder that was in the way or the rotten branch that broke or to some failure of co-ordination on the part of the victim. Instead, the accident, as one may loosely call it, is attributed to the act of a sorcerer.

Among the Australian aborigines, for instance, as among many other isolated peoples, death is never regarded as due to natural causes but is always ascribed to sorcery. With the assistance of a medicine man, the person responsible for causing the death is then usually discovered and subsequently becomes marked for death.

Since the magical practices of the sorcerer are, to a large extent, part and parcel of the religious system of groups, it will be readily understood that religion and primitive medicine are closely associated with one another — an association that in civilized societies has been attenuated but never quite dissolved.

With few exceptions, the diagnosis, treatment and prognosis of disease are all made by the medicine man, and when he is able to discover the cause, as he usually is, he can generally neutralize the effects of the maleficent spirits by some countermagic. When the disease object is capable of being abstracted directly from the victim's body, such abstraction is a simple matter for an expert medicine man. It is only in certain cases of breach of taboo that he, or anyone else, can do nothing.

Breach of Taboo

Taboo (originally a Polynesian word) may be defined as a prohibition the infringement of which automatically brings about its own punishment. Certain things are regarded as in themselves so dangerous that to break the taboo in connection with them results automatically in punishment without the mediation of supernatural or human forces. The occult power residing in a mystically dangerous object is transmissible and is therefore capable of affecting whatever comes into contact with it. The contact that most frequently automatically releases the occult punishing power is bodily contact. In many parts of Africa it is forbidden to touch anything from which the king or chief has eaten, be it the food or the plate from which it was taken. Anyone who willingly or unwittingly breaks this taboo is inescapably doomed to die, usually within a few days to a few weeks. So powerful is the force of suggestion here that the native who has broken the taboo often wastes away from no apparent cause.

The phenomenon of what has been called "voodoo death" is so interesting that a few words in explanation of the mechanism may be offered here. The evidence strongly suggests that death in such cases is due to the action of the sympathicoadrenal system in producing a marked decrease in blood pressure similar to that seen in wound shock. The blood volume is reduced until it becomes insufficient for the maintenance of an adequate circulation. Cannon[19] writes:

> Thereupon deterioration occurs in the heart, and also in the nerve centers which hold the blood in moderate contraction. A vicious circle is thus established; the low blood pressure damages the very organs which are necessary for the maintenance of an adequate circulation, and as they are damaged they are less and less able to keep the blood circulating to an effective degree.

Constriction of the arterioles produces a dangerous fall in the oxygen supply of the capillaries of the

internal organs, the thin walls of which when they do not receive an adequate supply of oxygen become more and more permeable to the fluid part of the blood. Plasma escapes into the perivascular spaces, with a resulting high concentration of red corpuscles, and the victim dies of shock scarcely distinguishable from true wound shock.

To return to taboo, Webster [20] writes:

> The authority of a taboo is unmatched by that of any other prohibition. There is no reflection on it, no reasoning about it, no discussion of it. A taboo amounts simply to an imperative thou-shalt-not in the presence of the danger apprehended. That any breach of the prohibition was unintentional or well intentioned matters nothing; no allowance is made for either the ignorance or the praiseworthy purpose of the taboo-breaker.

When sickness is believed to be produced by the breach of some taboo, expiation of the offence may sometimes be made with the assistance of a medicine man, who, by the performance of certain magical acts, may succeed in releasing the victim from the effects of his transgression.

Disease-Object Intrusion

In isolated societies it is a widespread belief that many types of illness are caused by the entrance into the body of some foreign object. Such morbific objects may find their way into the body either by direct human agency or by the action of some nonhuman agent. The disease object is usually regarded as carrying a spiritual essence, which is the real cause of the illness. Under such conditions it becomes the function of the medicine man to extract this object from the victim's body. The disease object may take almost any form, but it is always extremely small — a pebble, a splinter of wood or bone, a hair, an insect, a lizard or a worm. Removal of the object is usually accompanied by sucking on some part of the body, and in a short time the medicine man produces the pathogenic object from his mouth. This has, of course, been secreted there by him for production at the appropriate time, in much the same manner as many a modern physician, called on to deal with a patient who mistakenly believes that a fishbone has lodged in his throat, produces a fishbone that was never there. In either case the patient leaves perfectly happy in the knowledge that he will be troubled no longer. Since in many cases the illness was originally produced by suggestion, the sight of the object believed to have been the immediate cause of the disease is sufficient to work a cure.

Spirit Intrusion

When it is believed that disease is due to the presence in the body of some immaterial agent, such as a spirit, a ghost or a demon, one may speak of disease by spirit intrusion. This must be carefully distinguished from spirit possession, the latter resting on the belief that a person has been entered by a supernatural being, who then speaks through his host. Such a person is not regarded as ill in the ordinary sense of the word. His insanity is, on the contrary, regarded as evidence that he has been honored by a supernatural being who has taken abode within the affected person's body. He is therefore respected as a holy one and is often consulted as an oracle.

There are three methods ordinarily used to eject the intrusive spirit from the victim's body — exorcism, mechanical extraction and transference. In exorcism, the evil spirit is ejected by conjuration. The spirit is removed by manipulative, surgical or similar means in mechanical extraction. Transference refers to the transfer of the disease object from the victim's body to some object. Exorcism is nearly always practiced together with one or both of the other methods.

Soul or Body Loss

Abstraction of the soul or a part of it or some part of the body is still another mode in which disease is believed to be produced. Among the Australian aborigines the abstraction of the kidney fat, or perhaps more correctly the fat of the greater omentum, is held to be a common cause of disease. It may be removed by sorcery as a punishment for the infringement, knowingly or unknowingly committed, of some rule, thus bringing about the death of the victim.[21] Still more widespread is the belief in soul abstraction as the cause of disease and often of death. The soul may be abstracted by ghosts or sorcerers, or during sleep the soul may leave the body — as it is frequently believed to do in dreams — and meet with some accident on its nocturnal wanderings that prevents its return. The task of the medicine man is to discover the whereabouts of the missing soul by divination or other means and return it into the body of his patient.

Dreaming

Dreams may be the cause of sickness. In the Pacific and in the southwestern areas of North America, one may dream that one has eaten poisoned foods or that an animal has entered one's body, and wake up or fall ill shortly afterward. Furthermore, the dreamer may not himself suffer from the dream, but a relative of his may be afflicted.

Independent Occurrence

Minor ailments, such as leg sores, cuts, scratches and a host of other minor conditions, are regarded as arising independently of any action on the part of human beings or of higher powers. It is when a disease appears to threaten life that people begin to think of human or spiritual agencies. Attracting little attention, minor ailments do not afford material for speculation. When Rivers[12] inquired of the Eddystone islanders of Melanesia what caused these minor ailments, they replied that they came of themselves and were not, therefore, the occasion

of rites such as naturally follow disease ascribed to the neglect of religious injunctions.

Such minor ailments do not, therefore, necessarily fall into the domain of what would be called natural causation. Since they are unimportant, no one thinks enough of them to attribute them to any cause, and since they do not require any appeal to magical or spiritual agencies for cure, they are treated with domestic remedies.

Primitive Medical Practice

A brief account of some of the more practical devices to which isolated man resorts in various parts of the world will serve to convey some idea of his ingenuity and the closeness of many of his practices to modern ones, or even their identity with them.

Among the Ashanti of West Africa, inoculation for smallpox or against snakebite is successfully undertaken. In smallpox, the contents of a pustule are rubbed into an incision made in the skin. In the treatment for snakebite, the procedure is almost identical with the most recently devised methods. Veins are punctured by the use of splinters of stone or bone or by the use of a little arrow, which is shot into the vein from a miniature bow. Cupping and bloodletting are widely practiced; cupping is usually carried out by powerful suction with the mouth through a bone tube or similar instrument. Drainage from wounds is sometimes secured by means of sections of bamboo. Foreign bodies are extracted and abscesses opened with a thorn or a sharp-pointed instrument.

Suture or tight bandaging to promote union is not unknown among some tribes. Stitching of small wounds is carried out by means of thorns. A highly original method of suturing a wound is practiced among certain Indian tribes of Brazil. Both edges of the wound are allowed to be seized and brought together by the sharp head-nippers of certain ants, whose bodies are then rapidly cut off; one ant after another is used until the wound is closed.

Ulcers are frequently treated by cauterization with hot ashes or with heated blades and irons. In the treatment of fractured bones, splints and occasionally casts made of clay are used. On the whole, the results obtained by the native bonesetters are said to be extremely good. Trephining of the skull has already been mentioned. At all times a serious operation, this is skillfully performed by the native surgeon with a blade of stone or glass. There are skulls in museum collections that show that persons have been operated on in this manner as many as four or even five times. Evidence of healing around the bone edges shows that there has been good recovery in these cases.

Medicines are given in the form of decoctions, poultices, embrocations, salves and infusions of various sorts. Hydrotherapy, dietetics and massage are widely practiced. Enemas are administered by means of primitive appliances, and fumigations, inhalations, snuffs, nasal douching and instillations are also more or less widely practiced. This list of medical practices could be widely extended, but enough has been said, it is hoped, to indicate that the medical resourcefulness of isolated man is scarcely less than our own.

A few words may be added concerning the medicine man. How does a person become a medicine man? The pattern varies with different peoples. In some tribes the position is hereditary; in others the addiction to epileptiform states is the best qualification, or a man may come to be recognized as possessing a special gift for setting broken bones. In still other tribes the would-be medicine man must undergo a special course of training, and in certain societies there are even distinct grades of medicine men — for example, among the central Australian aborigines. Here the three grades of medicine men are those who are made by the spirits, those who are made by a special class of mischievous spirits and those who are initiated by other medicine men. The first two grades are more highly regarded than is the third. In each case the man himself believes that he is especially capable of becoming a medicine man. Women may become medicine women in the same manner. Practically everywhere women are the midwives and child doctors. Among the American Indians one may become a medicine man in a variety of different ways. Among the central Algonquin peoples, for example, there still exists a secret society known as the Midewiwin. This society is the repository of most of the medical knowledge of the tribe — a sort of college of physicians — into which one may gain entry by apprenticeship in early youth or by payment of the necessary fees and acquisition of the proper knowledge at any later time. It is a great honor to be a graduate of the Midewiwin. Different degrees of medicine men are recognized, according to the type of initiation they have undergone, and there are different types of specialists in the various disorders to which man is heir.

In many other cultures a person becomes qualified to treat a disease by virtue of the fact that he himself has recovered from that disease. In Africa a man may become a doctor by apprenticing himself, for several years and at an appreciable fee, to an already established medicine man, who then teaches him what he should know. A graduate medicine man may go in for postgraduate work by purchasing still higher secrets from others whose practice has brought them great renown.

* * *

From this presentation of the concepts of disease held by isolated peoples it will be seen that their medic ne represents a perfectly rational system. Their medical practices are a most logical conse-

quence of the spiritistic beliefs that such peoples hold. Their ideas of causation may be wrong from our standpoint, or they may contain a grain of truth here and there, but given certain spiritistic concepts, the body of medical practice follows with a degree of consistency that we can only hope some day to equal. In short, it should be clear that, in his view of the nature of disease and its treatment, isolated man is no illogical unreasoning creature. He is, in fact, a thinker who, with the data at his disposal, does at least as well as we should do under similar circumstances. Let us, then, look on him with the respect and understanding that are his due.

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CLINICAL NOTE

URETERAL CATHETERIZATION

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From a discussion that was recently heard it is evident that a simple technic for catheterizing the ureters in the presence of a vesicovaginal fistula is not well known. I therefore call attention to a method that was successfully used a number of years ago.

It was desired to catheterize the ureters for their better identification during the closure of a high vesicovaginal fistula. Since the fistula was of moderately large size, it would have been impossible to distend the bladder enough for successful ureteral catheterization with the usual technic. The problem was solved by soldering a nasal atomizer tip over a flexible eustachian catheter, allowing the catheter to project slightly beyond the atomizer tip. The arrangement is seen in the accompanying illustration (Fig. 1). No doubt the cannula used in the Rubin test would have served equally well.

The tip of the eustachian catheter was inserted through the vagina and fistula into the bladder. The atomizer tip thus occluded the fistula. The fluid passing through the eustachian catheter quickly dilated the bladder, allowing easy catheterization of the ureters.

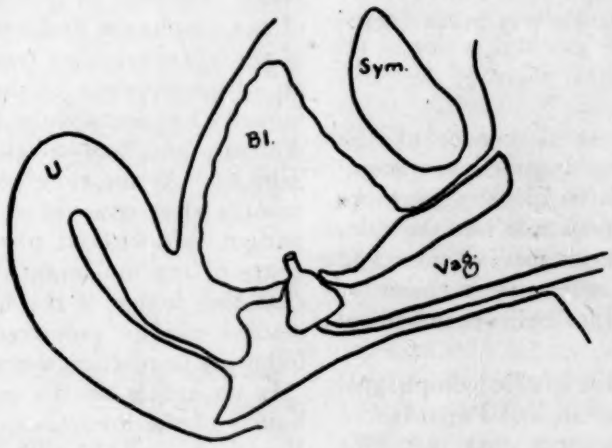

Figure 1.

*Surgeon, New England Sanitarium and Hospital.

MEDICAL PROGRESS

ENDOSCOPY (Concluded)*

EDWARD B. BENEDICT, M.D.†

BOSTON

ESOPHAGOSCOPY

Benign Tumor

Adams and Hoover[43] report 3 cases of benign tumor of the esophagus and include a review of the literature. Many of these tumors were incidental discoveries at autopsy. The number of cases discovered and recorded during the last eleven years owing to good x-ray technic and esophagoscopy is over half as large as the number of cases recorded in the preceding two hundred and twenty years. In a pathological classification of these tumors there were 35 polyps, 10 myomas, 9 papillomas, 8 fibromas, 6 cysts and 5 or less each lipomas, adenomas and unclassified tumors. There were 1 aberrant thyroid gland, 1 benign giant-cell tumor, 1 hemangioma, 1 lipomyoma, 1 neurofibroma and 1 osteochondroma. In 2 of the cases reported by the authors the tumors were removed by open operation; the third was removed with the aid of a suspension laryngoscope after the tumor had been drawn into the oral cavity by means of an esophageal speculum.

Harper and Tiscenco[44] have discussed benign tumor of the esophagus and its differential diagnosis. Benign tumors are relatively rare as compared with malignant tumors. The case reported is that of a benign intrinsic extramucosal tumor of the esophagus in which the diagnosis was made roentgenologically by exclusion.

Carcinoma

Borges[45] analyzed 153 cases of cancer of the esophagus. Ninety-nine cases received esophagoscopic examination, and positive biopsies were obtained in 83. Distant metastasis was not the rule; the lymph nodes in the posterior mediastinum and those about the left gastric artery were the most frequently involved. The author believes in radical resection whenever possible.

Tomlinson and Wilson[46] have studied esophageal carcinoma in British West Indian and Panamanian Negroes. Although recent reports state that this tumor is far more frequent in white males, especially in those of Jewish extraction, than in West Indian and Panamanian Negroes, the authors found 50 cases in Negroes, Indians and mestizos. In 50 cases studied at autopsy, the periesophageal lymph nodes were grossly invaded in every case. In British West Indian Negroes, carcinoma of the esophagus ranked third among all the types of carcinoma observed at autopsy.

Boros[47] states that carcinoma of the esophagus is one of the most frequent of all malignant diseases and is oftenest found in the male sex (75 per cent). Although his report, from the New York City Cancer Hospital, is extremely discouraging, the author mentions a glimmer of encouragement in the realm of radical surgery, referring in this connection to the work of Churchill and Sweet,[48] Wookey,[49] Garlock[50] and Ochsner and DeBakey.[51]

In an analysis of 599 cases of cancer, Toreson[52] found 19 cases of secondary involvement of the esophagus, an incidence of 3.2 per cent, 14 of the tumors originating in the breast, 2 in the pancreas, and 1 each in the testes and mediastinal lymph nodes; in 1 case the origin was undetermined. In 12 cases sufficient esophageal obstruction occurred to cause clinical symptoms. From this analysis, it is evident that secondary carcinoma of the esophagus is not infrequent and that dysphagia occurs in about half the cases.

An unusual case of multiple carcinomas was reported by Holland[53] in a fifty-five-year-old woman. In 1933 she had an adenocarcinoma of the right breast removed; in 1939 a squamous-cell carcinoma of the esophagus and a small basal-cell carcinoma of the left cheek were treated by x-ray; and in 1942 an adenocarcinoma of the colon (Grade 2) was removed. Incidentally, in 1943, she developed a mild diabetes and had a cholecystectomy for cholelithiasis. At the time of the report, twenty-eight months after removal of the fourth carcinoma, the patient was without physical or roentgen-ray evidence of any malignant disease. The author states that this is one of the first recorded cases of carcinoma of the esophagus with a five-year cure following irradiation therapy.

In an article on the surgical treatment of some lesions of the lower esophagus and upper stomach, Bradshaw and O'Neill[54] call attention to the fact that it has been stated that a positive biopsy must be secured before the operation is undertaken and, of course, is highly desirable in all types of surgery. On the other hand, small lesions in certain localities at the cardia are not readily accessible to the esophagoscope, gastroscope or fluoroscope. A valuable aid in such cases is the occurrence of spasm of the lower esophagus, which does not present the smooth

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coning seen in true idiopathic cardiospasm. Furthermore, the filling defect seen under the fluoroscope is not a true picture of the extent of the growth. The lesion may appear to be inoperable or questionably inoperable, yet actually be a relatively small carcinoma with extensive spasm.

Meyer and Kozoll[55] in an editorial on gastrostomy reviewed the records of 80 patients on whom gastrostomies were performed between 1941 and 1944. Forty-three patients died within two months of the performance of the gastrostomy. As these authors point out, such results speak for the futility of gastrostomy, even as a preliminary procedure, in resection of the esophagus.

I believe that most patients with carcinoma of the esophagus do not need a gastrostomy, either as a preliminary or a palliative procedure. A few of these cases can be determined to be inoperable by inspection of the liver with the peritoneoscope, and others are found to be inoperable at the time of exploratory thoracotomy. In those that are operable the problem of gastrostomy does not arise because the stomach is mobilized and anastomosed directly to the end of the esophagus. In those that are inoperable the patient's nutrition can in many cases be fairly well maintained by bougienage, with a previously swallowed thread used as a guide. Such patients are also given x-ray treatment.

In cases of carcinoma of the esophagus and in those of carcinoma of the stomach invading the cardia, Sweet[56] believes that direct inspection of the growth through the esophagoscope assists in making a correct diagnosis. A biopsy should always be obtained at such an examination and usually confirms the existence of carcinoma. The extent of the growth in the deep layers of the esophageal wall, however, cannot be determined by this method. Roentgen-ray visualization is of greater value for this purpose and gives more accurate information. Because of the frequency of direct invasion of the left main bronchus by the tumor in cases of carcinoma of the midesophagus, it is imperative to perform a bronchoscopy in all such cases. In this way an unnecessary exploration of the tumor through the chest may be avoided.

Benign Stricture

Clark and Adams[57] have reported 5 cases of transthoracic esophagogastrostomy for benign stricture of the lower esophagus. There were no deaths. In selected cases, transthoracic esophagogastrostomy offers the patient complete relief of symptoms without the necessity of repeated dilatations or the unpleasantness of a gastrostomy. None of the 5 patients were considered to have cardiospasm. In 1 case the stricture followed the ingestion of lye; in another it was associated with generalized scleroderma; and in 3 cases no etiologic factor could be ascertained.

Cardiospasm

Field[58] compares the effects of amyl nitrite, glyceryl trinitrate and octyl nitrite on achalasia of the cardia in 5 children. He reports that octyl nitrite relaxed the cardia and produced clinical improvement in 4 cases. The fifth patient failed to respond and on further investigation was found to be suffering from congenital stricture of the lower end of the esophagus. Field states that octyl nitrite is superior to amyl nitrite because its odor is pleasanter and less pungent than that of amyl nitrite, because it is less volatile and can thus be administered in an inhaler, which is a much more convenient form, and because clinically it produces relief and stops vomiting, whereas amyl nitrite often produces nausea and vomiting. The advantages of octyl nitrite over glyceryl trinitrate tablets or liquor glyceryl trinitrate are as follows: it is quicker in action, allowing less chance for food to be vomited; the necessary relief can easily be regulated by inhalations, according to the esophageal sensations felt by the patient; and clinically it produces relief and stops vomiting, whereas the vomiting continues under treatment with the other nitrites. The Octrite Inhaler* is a glass tube, with a vulcanite cap at each end, containing cellulose pellets impregnated with octyl nitrite. During use, both caps are removed and the inhaler is applied to one nostril, the other being closed. The author states: "The child now approaches his meals with the certainty that he can take them. No longer is he in fear that a heavy discomfort in the chest will bring eating to a stop, for he knows that this can be relieved without fuss by a sniff from the inhaler." The life of the inhaler tube varies from seven to twenty-eight days. The author further states that octyl nitrite inhalation also produced favorable results in adults suffering from cardiac achalasia.

Clagett, Moersch and Fischer[59] point out that the vast majority of patients who have cardiospasm obtain excellent results from dilatation of the cardia by means of the hydrostatic dilator, and that it is only in the exceptional case that surgical intervention becomes necessary. Approximately 70 per cent of these patients are completely relieved by one course of treatment. In 30 per cent of cases there is a tendency for the condition to recur. The recurrence may take place at any time from immediately after treatment to twenty-five years after it. If the condition does recur, the great majority of patients can be successfully relieved by subsequent dilatation. Dilatation of the esophagus by means of the hydrostatic dilator can be employed with little risk, in these authors' experience the risk having been less than 0.1 per cent. In 2 to 5 per cent of cases hydrostatic dilatation does not prove efficacious and surgical intervention is indicated. Of the surgical procedures that have been recom-

*Obtainable from Hynson, Westcott and Dunning, Incorporated, Baltimore.

mended, the authors prefer esophagogastrostomy performed through a transabdominal approach. A review of the literature and the authors' results indicate that this is a safe procedure that accomplishes good results. Although good functional results are obtained, one should not expect retrogression in size of the dilated esophagus after the operation.

I believe that the value of surgical procedures for cardiospasm is still unproved. Sometimes the results are not satisfactory, especially when operation is undertaken without an adequate trial of dilatation with the mercury bougie or with the hydrostatic dilator in experienced hands.

Scott[60] has analyzed 85 cases of idiopathic dilatation of the esophagus — usually diagnosed as achalasia of the cardia or as cardiospasm. Aided by the information obtained from the use of spinal anesthesia as a tool of investigation, he believes that it is possible to recognize four different clinical types, which probably also differ from each other in their etiology. These types are achalasia of the esophagus, true cardiospasm, dilatation associated with a constriction at or just above the cardia and dolichoesophagus. In conclusion, Scott states that achalasia is probably the most frequent type. It usually responds well to dilatation. In true cardiospasm the reflex originating focus should be discovered and removed. Those cases caused by a partial constricting band near the cardia are few in number but are probably resistant to conservative treatment. Dolichoesophagus — an S-shaped lengthening with pooling of esophageal contents at different levels — should probably be operated on immediately on recognition. This type is extremely difficult to control when the dilatation becomes gigantic and is complicated by infection of the esophageal wall. Subdiaphragmatic esophagogastrostomy — of the Finney pyloroplasty type — appears to be the operation of choice in those cases of idiopathic dilatation of the esophagus that are resistant to the usual conservative measures. The symptomatic results of this operation are usually excellent, whether or not the dilatation of the esophagus is entirely corrected. The danger of the operation is not excessive when proper precautions are taken. After it has been employed more extensively, the number of cases in which it is indicated will probably be considerably increased, but it should never replace conservative dilatation in the majority of cases.

Weens[61] calls attention to the frequent association of pulmonary disease with megaesophagus. In 3 cases the respiratory symptoms had completely overshadowed the digestive disturbances so that the presence of the megaesophagus was almost missed. It is this author's opinion that the pulmonary complications in megaesophagus are the result of aspiration into the bronchial tree of food particles regurgitated from the esophagus into the pharynx, as is so often noted in this condition.

Hawes and Soule[62] have reported 2 cases of severe cardiospasm associated with extensive pulmonary changes. One patient, a man aged fifty-seven, showed an interstitial fibrosis with cough and hemoptysis; the other, a man of thirty-one, manifested an increased density in the right upper lobe. The authors mention that patients with cardiospasms are often bothered with coughing and occasionally sudden paroxysms of strangulation, which are frequently precipitated by lying down. In the recumbent position the large reservoir of food and fluid may spill into the pharynx and be aspirated, and the patient may be aroused from his sleep by severe coughing. At times, the fluid entering the bronchi leads to pulmonary disease. Five types of pulmonary changes associated with cardiospasm have been observed roentgenologically — basal pneumonitis, lung abscess, bronchiectasis, pleural effusion and interstitial pulmonary fibrosis. In each of the 2 cases reported there was a long-standing asymptomatic pulmonary lesion, probably an interstitial fibrosis following aspirating pneumonitis.

Bird-Acosta[63] also calls attention to pulmonary suppuration as a result of esophageal overflow. Esophageal retention may be caused by carcinoma of the esophagus, strictures, foreign bodies, pulsion diverticulum, extrinsic esophageal pressure from adjacent tumors and cardiospasm. Of all the causes of pulmonary suppuration following esophageal overflow, cardiospasm, although a fairly common clinical entity, is rarely considered. The author reports 3 cases of pulmonary suppuration as a result of cardiospasm.

Cardioesophageal Relaxation

A case of cardioesophageal relaxation is presented by Berk.[64] It was diagnosed by roentgen-ray examination and confirmed by esophagoscopy. Cardioesophageal relaxation, or insufficiency of the cardia, is an abnormality of unknown etiology in which gastric contents regurgitate passively into the esophagus through a patulous cardiac sphincter. It may be looked on as the direct antithesis of achalasia (cardiospasm). In this case careful x-ray studies were carried out in which it was concluded that there was no herniation of the stomach but simply a relaxation of the cardioesophageal junction. Esophagoscopy disclosed the esophagus to be dilated and flabby. No true hiatus hernia was seen, and no gastric mucosa. The impression of the esophagoscopist was insufficiency of the cardiac sphincter. The chief symptoms of this disease are epigastric distress and a lumpy sensation at the lower sternum.

Ulcer

The case of a thirteen-week-old male infant with traumatic esophageal ulcer has been reported in the

Case Records of the Massachusetts General Hospital. In discussing this case Castleman,[65] the pathologist, stated his belief that the entire difficulty was related to the use of the gavage tube before the patient entered the hospital. The patient was the first of twins born seven weeks prematurely. The birth weight was 3 pounds, 1 ounce. The other twin weighed 2 pounds. Both children vomited frequently, and the other child died after one week. The patient was fed human milk by gavage many times while in the hospital. In the clinical discussion Farber[65] noted that gavage feeding of premature babies is frequently a necessity and saves many lives. It may be the cause of ulceration of the esophagus, however, particularly when the feedings are performed by inexperienced people. Such ulceration may form the starting point for infection, which may end in bacteremia. Pathologically, it was believed that the pulmonary lesions were almost certainly due to aspiration of the vomitus, which must have been mostly milk. It is also possible that at times some of the food fed by the gavage tube slipped down the larynx.

Rankin[66] reports a perforated ulcer of the esophagus following a burn. In 1842, Curling first described as a clinical entity an ulcer of the duodenum following a burn. To this day the etiology remains unknown.

The most popular theories for ulcer following burn are those of action of a burn toxin, stasis due to blood concentration, stasis due to low blood volume and adrenal activity, the embolic theory, the septic theory, the hypothalamus theory, the autonomic theory and the theory of nutritional disturbance. These ulcers are extremely rare, occur most frequently in children, perhaps reflect a severe toxemia, are seldom recognized during life and in general are an enigma in the medical literature. A case of perforated so-called "Curling's ulcer" of the esophagus with hemorrhage is reported. This occurred in a boy aged four years who had received second-degree burns to his thighs, buttocks and abdomen two days before admission to a hospital and died a few hours after it. Although none of these cases have been treated surgically, the only hope for the patient lies in immediate operation.

Smithers[67] has made a study of short esophagus (thoracic stomach) and its association with peptic ulceration and cancer. He first gives a historical sketch of congenital short esophagus and then discusses the theories regarding the association of thoracic stomach with peptic ulceration of the esophagus. Finding objections to the theories of congenital short esophagus and of fibrosis and constriction, he puts forward his own theory as follows:

> Congenitally short oesophagus is rare . . . , being seldom found at autopsy. Many cases so diagnosed during life have an acquired or an apparent shortening, rarely demonstrable after death, and resulting from hiatus insufficiency, sometimes developmental, more often acquired in later life. . . . With the cardiac sphincter in the thorax, released from any diaphragmatic control, gastric juice tends to flow into the oesophagus predisposing to peptic ulceration. . . . Irritation of the oesophageal mucosa by gastric juice (or probably by oesophagitis from any cause) may produce irregular spasmodic contraction of the lower end of the oesophagus . . . , which frequently appears, not only as irregular constrictions from side to side, but as longitudinal contraction or shortening. Relaxation of contraction and equalisation of pressure in the thorax and abdomen returns the herniated portion of the stomach to the abdomen by the time that a post-mortem examination is performed in cases where the oesophagus is of normal length. . . . Heterotopic gastric mucosa may secrete gastric juice into the oesophagus or the gastric contents may reach it in other ways (for example, as the result of vomiting, rumination, or relaxation of the cardia following operations) in patients without a lax hiatus. Peptic ulceration of the oesophagus may occur in these patients without radiological evidence of shortening of the oesophagus. This theory (hiatus insufficiency, congenital or acquired, first; spasmodic shortening of oesophagus and ulcer, second) accounts for the known facts and overcomes the chief difficulties associated with the "congenital short oesophagus" and "fibrosis and contraction" theories. A new explanation of the shortening of the oesophagus, so real to the radiologist and often apparent at oesophagoscopy, but so little known to the pathologist, seemed to be required. An upward spasmodic contraction of the longitudinal fibres of the oesophagus during life, with relaxation after death, has been implied as a possible explanation in the theory put forward above. It seems possible that irritation which will produce oesophagitis . . . or peptic ulceration of the oesophagus and irregular contraction of its lower portion . . . may result in sufficient spasmodic contraction of the longitudinal fibres to produce apparent shortening and to retain a portion of the stomach in the thorax during life.

The article also deals with the association of achalasia and short esophagus and hiatus hernia and cancer, as well as short esophagus and cancer. Smithers states that the association of cancer and short esophagus may be purely fortuitous and that more case reports must be awaited before one can do more than speculate on the possible influence of achalasia and peptic ulcer associated with thoracic stomach.

Esophageal Varices

Patterson and Rouse[68] have treated 12 patients with esophageal varices by the injection of sclerosing solutions. They believe that such varices serve no useful purpose that cannot be served by other and nonvulnerable anastomoses between the portal and systemic venous circulations. In their experience, obliteration of these veins results in no appreciable unfavorable effects; instead, clinical improvement occurs soon after prevention of blood loss from a ruptured varix. Eight cases are reported in detail.

Whipple[69] in a discussion on portal hypertension calls attention to the fact that attempts to ligate the tributaries feeding into the veins of the cardia and esophageal varices have been extremely disappointing. Nor have the injection and coagulation methods to obliterate the esophageal varices been any better. At best, these procedures shut off one of the chief collaterals between the portal and systemic circuits and increase the portal hypertension. Using a vitallium tube, Whipple and

Blakemore have carried out vein anastomoses in 10 cases, half consisting of uniting the splenic vein and the left renal vein after removing the spleen and left kidney. In 5 other patients they have anastomosed the portal vein to the inferior vena cava. Whipple states that these procedures are as yet purely experimental. He quotes Blalock[70] as having performed splenorenal vein anastomoses for portal hypertension in 4 cases, in 2 of which there was a disappearance of ascites and remarkable improvement. On the other hand, Blalock's enthusiasm is somewhat curbed because the other 2 patients have died since operation from recurrent bleeding from esophageal varices.

In a description of the technic of using vitallium tubes in establishing portacaval shunts, Blakemore and Lord[71] state in conclusion:

> Every one of the 10 cases of portacaval shunts went through a successful postoperative convalescence. The interval following operation has been too short in some to judge the results. However, in 6 of the 10 cases the improvement has already been so outstanding as to justify continuing the procedure. The Eck fistula operation is better tolerated by the patient, probably because of less blood loss during the procedure.

Lye Stricture

For esophageal poisoning due to lye Crowe[72] believes in the Bokay prophylactic therapy, using a No. 10 Fr. eyeless catheter filled with lead or mercury and tied off at the open end. It should be wet with water or a lubricating jelly, gently passed down the esophagus and left in place for five minutes daily, starting on the third day after the patient has swallowed the lye. The size of the catheter should be increased until difficulty is encountered in passing it.

Pellagra

Fisher[73] discusses the findings in 17 patients ill with pellagra, all of whom had a characteristic glossitis. Marked dysphagia was frequent. Esophagoscopy revealed an intensive hyperemia and in some cases edematous mucosa. Multiple tiny ulcerations of the esophageal mucosa were noted in 9 cases. Barium studies of the esophagus in 8 cases showed many small, constricted areas along its course. Following the daily administration of 150 mg. of nicotinamide, 15 mg. of thiamin chloride and 15 mg. of riboflavin, the patients could swallow solid food without experiencing dysphagia in from three weeks to two months. There was progressive improvement in the objective findings and clinical symptoms.

Foreign Body

Richardson[74] reports 17 cases of esophageal obstruction due to impacted meat. Twelve of the patients had no teeth of their own, and several of the others had very poor teeth. Six patients had a normal esophagus, but the other 11 had a narrowing or constriction of some portion. Spontaneous recovery can occur but is rare. Esophagoscopy may not be necessary if caroid or papain is used in a 5 per cent solution to dissolve the impacted meat.

Fistula

Abbott,[75] in an article on abnormal esophageal communications and their types, diagnosis and therapy, concludes that abnormal fistulous communications may occur from the esophagus into the bronchial tree, pleural cavity, mediastinum, pericardium and more remote tissue spaces. An esophageal fistula presents a serious hazard to the patient's life but not necessarily a hopeless one. This report adds 6 permanent closures to the 15 previously recorded. A review of the literature and a description of 23 additional cases is given. Two unusual cases of esophagopericardial fistulas are included in these reports. Another case, in which a fistula between the esophagus and the trachea occurred in association with Hodgkin's disease, is described, and this communication was successfully treated. To Abbott's knowledge, no previous similar cases have been reported. The symptomatology and diagnostic methods are described. The management of an esophageal fistula demands acute interest in methods of the patient's nutrition and the employment of early adequate drainage. Some fistulas close spontaneously under this regimen alone. Direct surgical attack on esophageal fistulas is applicable in some cases but can sometimes be obviated by endoscopic topical applications.

Abbott has reviewed 22 cases of abnormal esophageal communication that have been handled at the Barnes Hospital. The predominating cause was found to be malignant lesions of the esophagus or larynx. These constituted 13 of the 22 cases reported, and another case occurred in association with Hodgkin's disease. Two fistulas were secondary to chronic empyema, 2 were secondary to operative procedures, and 2 were associated with syphilitic aortic aneurysms. One patient developed a fistula following instrumentation, and another developed one in association with a congenital diverticulum of the esophagus, instrumentation having been used in this patient. No examples of fistulas in relation to tuberculous empyema or tuberculous mediastinal lymphadenitis are contained in this report. This is due, at least in part, to the fact that patients with chronic tuberculosis are usually relegated to sanatoriums. The diagnostic measure of the greatest value consists of x-ray visualization of the fistula, preferably with iodized oil to prevent barium irritation of the lung parenchyma. Considerable difficulty may be encountered in trying to visualize these communications directly with the aid of the esophagoscope, but the instillation of methylene blue within the esophageal lumen followed by bronchoscopic examination can be a helpful measure.

Moersch and Tinney[76] have found that the most frequent site of acquired fistula between the esophagus and the trachea or bronchi is at or just above the bifurcation of the trachea. The left main bronchus is involved oftener than the right. Carcinoma of the esophagus was found to be the most frequent cause of this type of fistula, accounting for 36 per cent of 39 cases. Rarer causes were trauma, syphilis, tuberculosis and esophageal diverticulum, with a number of causes responsible for single cases. The etiology was unknown, however, in several cases. The clinical findings were found to depend on the primary pathologic changes and the size and location of the sinus tract. In esophageal cancer, the development of the fistula is suggested when, after a period of dysphagia, the ingestion of food is followed by cough, expectoration and dyspnea. This occurs particularly after taking liquids. X-ray study after the ingestion of iodized oil usually demonstrates the lesion. Because of the nature of the underlying disease, the prognosis is usually poor, and the cancer itself or pneumonia or mediastinal or lung abscess causes death. Small fistulas due to trauma may, however, last for years. In these cases surgical repair may be of value.

Haight[77] has presented the anatomic and surgical problems concerned with the correction of congenital atresia of the esophagus with tracheoesophageal fistula. Reconstruction of esophageal continuity by a single-stage operation consisting of an extrapleural closure of the tracheoesophageal fistula and an anastomosis of the esophageal segments offers the most satisfactory approach to the correction of the anomaly. A primary anastomosis of the upper and lower esophageal segments was done in 16 of the 24 patients on whom an exploration was undertaken. Six of the 16 patients for whom an anastomosis was performed were living seven months to three years and one month after operation, and the reconstructed esophagus was patent in all cases.

Gastroscopy

Complications

Fletcher and Jones[78] report on the risks of gastroscopy with the flexible gastroscope, having had 2 fatalities in twenty-eight hundred gastroscopic examinations. In both cases the Herman Taylor gastroscope was used. This gastroscope has a longer rigid and shorter flexible portion than the Wolf–Schindler flexible gastroscope. Both these fatalities were believed to be due to an error in judgment. In the first case, gastroscopy was probably contraindicated, since the patient's tissues might have been expected to be in a fragile state as a result of recent scurvy. In the second case, extra pressure was exerted when the tip of the gastroscope was lying in the hypopharynx; such pressure should not have been applied. In addition to their own cases, Fletcher and Jones have heard of 5 other fatal cases. The Herman Taylor gastroscope was used in 5 of these 7 fatal cases. The authors call attention to the fact that gastroscopy with the flexible gastroscope is proving to be an indispensable means of diagnosis in diseases of the stomach and is rapidly becoming a routine procedure in almost every large hospital in the country. It is inevitable that many gastroscopies should be performed by inexperienced gastroscopists. They believe that beginners have a false sense of security in their use of the instrument, based on the rarity of reported accidents. It is important that all users of the flexible gastroscope should realize that there is a slight but definite risk associated with the passage of the instrument, and that in this, as in all endoscopic methods, the greatest circumspection is needed. These authors believe the main risk is that of perforation of the upper part of the esophagus and the hypopharynx. Both their deaths occurred in elderly women. They admit that the flexible part of the Herman Taylor gastroscope is 2 mm. wider and is appreciably stiffer than the corresponding part of the Wolf–Schindler apparatus and that extra care may be necessary for its passage into the esophagus. On the other hand, they believe that the Herman Taylor model gives a better view of the stomach than can be obtained with the Wolf–Schindler instrument, and they consider it the gastroscope of choice provided it is passed with care.

Schindler[79] reports a case in which an apparent rupture of the stomach occurred during gastroscopy and pneumoperitoneum developed. At operation three hours later no trace of a lesion was found, although the pneumoperitoneum was present. The patient recovered.

Gastroscopic Study

According to Renshaw,[80] the diagnostic study of many patients cannot be considered adequate and complete without gastroscopy, which is an office procedure. Contraindications for examination are chiefly diseases of the esophagus and mediastinum. The limitations of gastroscopy are few, the main one being the so-called "blind areas" of the stomach, which vary in size. The procedure is indicated in further study of patients with negative roentgenologic findings in whom gastric disease is suspected, for classification of many cases with indeterminate, suspicious or inconclusive roentgenologic findings and for elucidation of certain obscure conditions, such as unexplained gross hemorrhage and gastrointestinal allergy. Gastroscopy in combination with roentgenoscopy and study of gastric content removed by the fractional method of gastric analysis has made the diagnosis of organic disease of the stomach comparatively simple.

Hardt, Hufford and Raben[81] have made an analytical survey of patients examined gastroscopically and roentgenologically. One or more gastroscopic and roentgenologic examinations were performed

in 1132 patients who complained of symptoms suggesting the presence of gastroduodenal disease. The facts provided by the two methods were compared. The evidence conclusively demonstrates that gastroscopy should be performed before a definite diagnosis of normality can be made, since these authors' experience indicated that the gastroscope is the most efficient diagnostic aid in making a negative gastric diagnosis and in diagnosing all types of gastritis. In their experience, gastroscopy was superior to roentgenography in the diagnosis of all types of gastric ulcer, including marginal ulcers. The gastroscopist was correct in 89 per cent of all types of benign ulcerating lesions, and the roentgenologist correct in 58 per cent. The final stages of healing of the ulcer can be followed only by means of the gastroscope. Gastroscopy likewise is more accurate than roentgenography in localizing the ulcer and can detect earlier any changes suggesting malignancy. Some type of chronic gastritis was diagnosed gastroscopically in 19 per cent of 239 patients with duodenal ulcer, and gastroscopy thus added an important secondary diagnosis otherwise unobtainable. Gastric carcinoma was recognized gastroscopically in 94 per cent of the patients and by roentgenograms in 79 per cent; with a combination of both methods the lesion was detected in 98 per cent. Incomplete diagnosis gastroscopically occurred in 5 per cent, and the diagnosis had to rest entirely on the x-ray findings. On the basis of the authors' experience, gastroscopy is indicated in all cases of persistent or recurrent gastric complaints with negative roentgenologic findings in which the clinician still suspects the presence of gastric disease; in many cases of proved gastric ulcer in which operation is not performed but in which the lesion should be watched from time to time not only roentgenologically but gastroscopically; in cases in which the x-ray findings indicate a suspicious gastric lesion or in which a definite diagnosis cannot be made roentgenologically; and in all gastric carcinomas except those located at the cardia or well advanced in their course.

In 2 patients with negative gastrointestinal x-ray examination and negative gastroscopy, Hufford and Stonehouse[82] took roentgenograms of the Cameron–Schindler flexible gastroscope in the esophagus passing through the cardia and in various positions in the stomach. The degree of flexion of the gastroscope was greatest in the esophagus, and was of a lesser degree in the fundus of the stomach just below the cardia. The flexible rubber tip of the gastroscope flexes acutely to the left and slightly forward as it passes through the hiatus esophagus into the cardia. The blind spots in the gastric wall are the parts that are in contact with or short of the focusing distance from the objective or inclined away at such an oblique angle that only a darkened area can be seen. The action of this gastroscope as recorded by the roentgenograms is shown to be sufficiently flexible to pass through the normal anatomical channels without any undue stress or strain. The air inflated into the stomach during gastroscopic examination casts an identifiable shadow on the roentgenograms and unless eructated flows freely from the stomach through the pylorus, which shows satisfactorily the antral end of the stomach with peristaltic waves and a fairly good duodenal bulb. This report is well illustrated by eight roentgenograms.

From the beginning of World War II until December, 1943, Tanner[83] performed twenty-two hundred gastroscopic examinations on 1738 patients. In his clinic, the main use of gastroscopy was for diagnosis and observation of gastric ulcer. Of 631 cases of gastric ulcer, 159 were diagnosed solely by gastroscopy, since they apparently yielded normal x-ray findings. There are several reasons for the difficulty in diagnosis of many of the gastric ulcers by x-ray. For example, an acute ulcer may be too shallow to retain barium, or after a hemorrhage its base may be filled with blood clot, which prevents the entry of barium to the crater, or there may have been considerable delay after hemorrhage in x-ray examination of the patients, during which time the ulcer heals and the scarring may be missed roentgenologically. Thirty-nine of the patients with duodenal ulcer in this series also had a gastric ulcer, and cancer was also seen in 2 cases on which duodenal ulcer alone was suspected roentgenologically. Tanner agrees that even direct visualization of an excised ulcer of the stomach may not abide the truth as to its innocence or malignancy. Nevertheless, he writes, one is rarely in doubt after gastroscopic visualization, because vitality appears to accentuate the differences, and where such doubt exists a second inspection after ten days of medical treatment usually gives the clue. Certainly it is well worth while to examine gastroscopically every patient with an ulcer that is not healing rapidly under medical management. Superficial types of cancer may be missed roentgenologically. In this series there were 13 cases of cancer that had been considered benign or had not even been diagnosed roentgenologically.

Gastritis

Cutler and Walther[84] have reported on the significance of chronic gastritis in an Army general hospital, stating that a wide difference of opinion still exists on the clinical significance of the gastroscopic findings of chronic gastritis. They studied 333 soldiers. In conclusion they state:

> The gastroscopic surveys of asymptomatic subjects in this study and those by other workers have indicated that gastric mucosal changes can occur in symptom-free individuals. Notwithstanding, chronic gastritis is much more prevalent in the group of patients who do complain of chronic upper abdominal distress. In our series of such cases the incidence of chronic gastritis compares closely with the estimates of other workers previously cited. The frequent association of gastritis with duodenal

ulcer has again been corroborated in this study. The routinely uneventful response of these patients to an ulcer regimen does not militate against the symptomatic significance of chronic gastritis, for the ulcer syndrome may be mimicked rather closely by patients who have chronic gastritis alone. Apart from the hypertrophic group simulating peptic ulcer a large group of patients with chronic gastritis show no uniform symptom complex. Because of the frequency of associated complaints unrelated to the patient's gastrointestinal system it is difficult to believe that a chronic gastritis can alone play the leading etiologic role. A sampling of consecutive cases of chronic gastritis has demonstrated the predominance of psychogenic factors. The possibility therefore arises that the gastric mucosa by its organic changes points to a more basic disturbance of psychiatric importance.

Holtermann and Myhre[85] in a discussion of gastritis state that gastritis was present in every case of duodenal ulcer and was generally more pronounced and diffused than in gastric ulcer. Gastroscopy is the most reliable diagnostic method and may likewise aid in classification. The gastritis may also be demonstrated roentgenologically. Better information will be obtained when small amounts of contrast medium are spread evenly over the mucosa. Negative roentgenologic findings do not exclude gastritis. Differential diagnosis between hypertrophic gastritis and superficial catarrh and atrophy should not be based on roentgenologic findings.

Hypertrophic Gastritis Simulating Tumor

Pollard and Cooper[86] made observations of 8 patients in whom stomach x-ray films revealed a filling defect similar to that seen in carcinoma. All the patients were men, and their ages ranged from twenty-two to sixty-five years. In all but 2 cases subjected to gastroscopy, the diagnosis of localized hypertrophic gastritis was established with reasonable certainty by this method of examination. The diagnosis of hypertrophic gastritis and the absence of neoplasm was confirmed in 7 cases by laparotomy and in 6 cases by histologic examination of removed tissue. Since early diagnosis and treatment are essential in the management of gastric neoplasm and operation may be contraindicated in cases of hypertrophic gastritis, it seems important that all these cases be examined gastroscopically before surgery is undertaken. Furthermore, it is perhaps wiser not to depend on a trial of conservative therapy to establish the diagnosis. Localized hypertrophic gastritis is capable of producing a filling defect in the stomach that is difficult to distinguish roentgenographically from that of carcinoma. The symptoms of hypertrophic gastritis may be indistinguishable from those of peptic ulcer or gastric carcinoma. Neither roentgen-ray nor gastroscopic findings are enough in themselves to enable one to distinguish between localized hypertrophic gastritis of the lower regions of the stomach and annular neoplasm in that area.

Hinkel[87] has reported an interesting case of a localized hypertrophic gastritis simulating the roentgen-ray picture of a tumor. His case revealed a neoplastic type of filling defect on the lesser curvature of the cardia of the stomach. The tumor-like filling defect was also demonstrated, following pneumogastry, as a soft-tissue mass protruding into the gas bubble. The author discusses the differential diagnosis and briefly cites some of the literature on this subject. He points out that the protruding mass of the pseudotumor is due to a piling up and crowding of the hypertrophic redundant inflammatory mucosa. He emphasizes that achlorhydria is strikingly frequent in this form of gastritis.

Postoperative Gastritis

Browne and McHardy[88] limit their discussion to chronic postoperative gastritis. They point out the difficulty of a clinical diagnosis following gastrectomy, since this type of gastritis may mimic many gastroenteric lesions. Gastroscopy is suggested. Subclassification is limited to superficial, hypertrophic and rarely atrophic gastritis. The degree of redness of the mucosa was related to the hematopoietic status of the patient. A combination of the first two classifications was frequently encountered; it was severer in the anastomotic area, extending even into the jejunum. An accurate description of the findings is given. Causative factors such as chronic illness, severe trauma, achlorhydria and improper dietary regulations are given instead of the bacteriological factors. The authors give an optimistic prognosis, and after finding roentgen-ray therapy unsatisfactory, they suggest an ulcer regime supplemented by vitamins and liver extract. A case is reported.

Christiansen[89] believes that postoperative gastritis is a special form of gastritis, differing from other forms in its clinical picture as well as in its pathological and gastroscopic aspects. Gastroscopy reveals an extremely polymorphous picture, which is characterized by a mixture of superficial, hypertrophic, atrophic, erosive and ulcerative lesions. The clinical symptoms differ in many respects from those of peptic ulcer — for instance, the pain is not relieved by food intake. The question of pathogenesis is open to argument, and different theories are discussed.

Gastric Ulcer

Freeman[90] believes in the gastroscopic control of the treatment of gastric ulcer by duodenal feeding. Although roentgenography is still the standard method of choice in the diagnosis of an ulcer, this author has found a number of ulcers by gastroscopy that were missed by the radiologist; this may have been accounted for by failure of the barium to fill the crater because the floor was already filled with slough of mucus. Therefore, patients who present ulcer symptoms and in whom a negative x-ray examination has been reported should be examined with the gastroscope, and the examination should

be repeated subsequently before cessation of treatment is contemplated.

Carcinoma

In commenting on the relation between diet and cancer, Grossman and Ivy[91] raise the question of the possible relations between dietary irritants and gastritis and gastric cancer. They state:

> Cramer (1934) has observed that the total cancer rate is the same in England and Holland, though the incidence of cancer of the stomach in Holland is approximately twice as great as in England. A subsequent study of Lintott (1939) and Herbert and Bruske (1936) indicated that the Dutch people consume more roughage, hotter food and more spices, spirits and tobacco and have more oral sepsis than the English.

Stout[92] has made a study of gastric mucosal atrophy and carcinoma of the stomach. This study revealed that mucosal atrophy may appear as early as the third decade and is found with increasing frequency and extent in the succeeding decades of life. In comparable groups of stomachs mucosal atrophy is found in a large number and tends to be more widespread in those with cancer than in those without it. But when one tries to find actual progression from altered mucosal glands, gastric or intestinal in type, cystic or not, distorted or regular, it is realized that it is impossible to tell when there is juxtaposition of carcinoma and mucosal gland, whether the carcinoma is invading the gland or developing from its epithelial cells. In occasional stomachs with carcinoma multiple sections from various areas failed to show epithelial changes in some, whereas others showed only minimal changes. Although atrophy of the gastric mucosal epithelium and cyst formation were present to a greater degree and in larger numbers in stomachs with carcinoma than in comparable stomachs without it, the exact relation between these conditions remained undetermined.

Dailey and Miller[93] in a search for symptomless gastric cancer in 500 apparently healthy men of forty-five and over conclude that a survey of the general population in search of gastric cancer is not worth while. Studies of selected groups such as those with pernicious anemia should be expanded, since this seems a profitable approach to the problem.

In a discussion of Krukenberg tumors, Lowman and Kushlan[94] emphasize the importance of a gastrointestinal survey in cases of ovarian malignancy to determine if possible a primary source of the tumor in the digestive tract. They stress the importance of using every available means of diagnosis in the differentiation of early carcinoma of the stomach and benign gastric ulcer — that is, serial roentgenographic studies and gastroscopy. Gastric ulcer not responding to therapy with rapid and complete healing as demonstrated by x-ray and gastroscopy should be treated as malignant and resected early.

Sweet[56] believes that the use of the gastroscope is of limited value in cases of carcinoma of the stomach near or invading the cardia. In an occasional case in which the roentgen-ray examination is equivocal, inspection through the gastroscope may help to establish a correct diagnosis.

In a careful analysis of the data available for a ten-year period at the Massachusetts General Hospital, Allen[95] has found that 14 per cent of the patients treated as having benign gastric ulcer proved to have cancer. These patients responded well to conservative therapy at first, with disappearance of symptoms and a regaining of lost weight. The lesion often appeared to diminish in size on roentgen-ray and gastroscopic examinations. Consequently, Allen is afraid of conservative treatment. He believes that early radical surgery is indicated when a patient appears for treatment with an ulcer of the stomach in the prepyloric or fundal regions. If he is over forty years of age and has had symptoms for less than one year or if his ulcer is over 2 cm. in diameter, the same advice should be given. If the patient is young and has a small lesion or if the ulcer is superimposed on symptoms of more than five years' duration, a more conservative attitude is justifiable. This patient should not be treated in an ambulatory fashion, as is the usual practice in mild or early duodenal ulcer, but should be given the benefit of an adequate hospital regimen. If the ulcer remains even partially unhealed after one month of such therapy or if there is a return of ulceration one month after healing is apparent, the patient should be urged to submit to surgery.

Since the advent of liver therapy, Olson and Heck[96] had found a notable increase in the number of cases of carcinoma and polyps of the stomach in cases of pernicious anemia. Undoubtedly it is significant that patients who have pernicious anemia now have an indefinite prolongation of life. The processes that are active in the alteration of the gastric mucosa are permitted by this extension of life to continue for many years. This factor is probably the one that is responsible for the increased incidence of polyps and carcinoma of the stomach. Pernicious anemia is a disease of the gastric mucosa as well as a disorder of the hematologic and neurologic systems. Treatment that is sufficient for the maintenance of normal blood may not be adequate to prevent atrophic changes in the gastric mucosa, which in pernicious anemia may not only become atrophic but may produce benign and malignant growths.

In a study of pernicious anemia and the early diagnosis of tumors of the stomach, Rigler, Kaplan and Fink[97] state that despite the expansion of roentgen-ray diagnosis, the more general use of gastroscopy and the refinement of the methods of examination of the gastric contents and stool, the record is a black one. The over-all salvage of only 2 per cent of the patients afflicted with this disease

or even the survival of 6 per cent, which is the maximum reported, gives a picture of the difficulties involved. The importance of gastroscopy is emphasized in the case of a patient with pernicious anemia and a benign polyp 4 mm. in diameter not found on the first x-ray examination but discovered gastroscopically and later confirmed by x-ray. The possibility of the malignant degeneration of a polyp should be particularly brought to mind in cases of pernicious anemia because of the tendency of the latter to develop carcinoma. In 1939, Rigler, Kaplan and Fink[97] undertook to examine roentgenographically all their patients with pernicious anemia at semiannual intervals. In summary, they state that in a roentgen-ray study of 211 patients with pernicious anemia on whom examinations of the stomach were made on one or more occasions, carcinoma of the stomach was found in 8 per cent and benign polyps in 7 per cent. In an autopsy study, reported elsewhere,[98] 12 per cent of patients with pernicious anemia were found also to have carcinoma of the stomach. The data presented indicate clearly an etiologic rather than an accidental relation between pernicious anemia and tumors of the stomach. The routine roentgen-ray examination of the stomachs of patients with pernicious anemia has proved to be a valuable procedure resulting in the salvage of some cancer cases that might otherwise not have been saved. Cases were observed illustrating the rapid change from a benign polyp to a cancer, the presence of both benign and malignant tumors side by side, the absence of symptoms in the presence of large tumors and the development from a small, barely detectable lesion to an extensive, inoperable carcinoma.

In a recent editorial, Benedict[99] states that a more accurate diagnosis can be obtained in the problem of gastric ulcer and carcinoma when all methods of examination are used in a given case than when reliance is placed on incomplete data. Gastroscopic examination supplements x-ray examination; it does not in any sense compete with it. Reliance can be placed on gastroscopic examination only when the method is carried out by an experienced gastroscopist who knows the limitations of the method, the relative blind areas in the stomach and the proper interpretation of his observations. In a recent lecture, Benedict[100] reported his study of 245 proved cases of gastric disease in an attempt to correlate the gastroscopic, x-ray and pathological findings. An analysis was made of 125 cases of proved carcinoma of the stomach in which it was shown that x-ray and gastroscopic examination were equally good in 67 cases and equally doubtful in 3 cases. X-ray examination was more accurate or more helpful in 32 cases, and gastroscopy was more accurate or more helpful in 20 cases. When the lesion was equally accessible to both methods of examination, the analysis indicated the relative superiority of gastroscopy over radiology in differentiating benign and malignant gastric ulcers. In the same report, 50 cases of proved benign gastric ulcer were analyzed. In 16 of these x-ray and gastroscopy were equally correct, in 9 cases they were equally doubtful, in 21 cases x-ray examination was superior to gastroscopy, and in only 4 cases gastroscopy was superior to x-ray. In both the carcinoma and the ulcer cases, gastroscopic failures were largely due to mechanical difficulties, which accounted for 25 of the 32 cases of x-ray superiority in the carcinoma group and for 17 of the 21 cases of x-ray superiority in the ulcer group. Benedict concludes that gastroscopy is of value in the ulcer-carcinoma problem and that the most accurate diagnostic results are obtained when all methods of study are used in combination.

Benign Tumor

According to Dewey,[101] the incidence of benign tumors of the stomach is estimated at 0.5 to 5.0 per cent of all gastric neoplasms. Adenomatous polyps are seven times more frequent in association with atrophic gastritis than in the presence of a normal mucosa. Diagnosis depends on roentgenologic and gastroscopic study, but the final determination is made by histologic examination. Early surgery is the proper treatment.

Gastric Mucosa in Hepatitis

Knight and Cogswell[102] examined by gastroscopy 9 patients with infectious hepatitis in 7 of whom the appearance of the mucosa was found to be abnormal. The area involved was always the anterior portion of the stomach, and in some cases the abnormal appearing areas extended into the fundus. The findings that have impressed these writers as being most distinctly abnormal gave the appearance through the gastroscope of being almost identical with the small aphthous ulcers that are often seen in the mouth. Five patients in this series were observed to have these ulcerations. Further study is essential before any conclusions can be formulated with regard to the relation between the findings in the gastric mucosa and infectious hepatitis.

Hemorrhage

From a study of 112 patients who had had gross bleeding from the upper gastrointestinal tract, Clark[103] advocates gastroscopic examination after hemorrhage of undetermined origin.

In an article on inflammatory lesions of the upper gastrointestinal tract, Aaron[104] suggests the following criteria for healing of ulcerated lesions of the stomach: complete cessation of all symptoms; maintenance of or gain in weight; persistent absence of occult blood from the feces; disappearance of anemia of the iron-deficiency and essential-factor type; a normal sedimentation rate; roentgenologic evidence of complete healing; and, if it is possible

to obtain it, confirmation by gastroscopy. Only when these studies are repeated over a four-week to six-week period of observation can one be sure that a lesion of the stomach has healed and remained healed and is thus likely to be benign. If this does not occur, the patient is entitled to surgical intervention.

Jankelson[105] has studied 60 cases of hematemesis of unexplained origin. Seven patients died before extensive studies could be carried out. In 3 of them, autopsy did not reveal the source of the bleeding. The other 53 patients had intensive posthemorrhage studies, including roentgen-ray examination in all cases and gastroscopy in 10 cases. In retrospect, Jankelson advocates earlier x-ray study as well as more frequent and earlier gastroscopic examination to demonstrate acute changes in the gastric mucosa, which often heal rapidly without leaving any permanent changes. Acute hemorrhagic gastritis, multiple fissures of the stomach and some gastric ulcers will thus be demonstrated.

Although 50 per cent of cases of chronic seasickness present x-ray evidence of hypersecretion, loss of gastric motility and spasm of the pylorus, as well as thickened gastric rugae in some, Benedict and Schwab[106] state that the gastroscopic picture is usually essentially normal.

Peritoneoscopy

In a report from the Memorial Hospital in New York City, Narancio, Pierson, McNeer and Pack[107] state:

> Our chief interest in this endoscopic field has been in the determination or recognition of the inoperability of various intra-abdominal neoplasms. One can frequently appreciate the inoperability of some cancers by this examination, but, on the contrary, the resectability can never be ascertained with any degree of certainty. If this fact were universally known, the limitations of the instrument would be accepted and no extravagant claims for its use would be made. . . . The chief indication for its use, in our hands, is the attempted determination of inoperability in borderline cases. . . .

Boehme[108] believes that peritoneoscopy has a definite and valuable place in the field of endoscopy. The enthusiasm for peritoneoscopy varies directly with the skill of the operator. Thus, also, the information gained on examination depends greatly on the skill and experience of the operator. Biopsy of the spleen was performed with some trepidation in 1 case. Only slight hemorrhage was encountered, and this was controlled by cautery. Fibrin foam was held in readiness, and it was intended to apply it to the bleeding surface by introducing it in the jaws of the biopsy forceps. This procedure should add a safety factor to biopsy of the spleen in the future. The indications for the use of peritoneoscopy to complete abdominal diagnosis are discussed. It is a safe, brief, relatively painless and valuable procedure. The anatomical and other limitations are reviewed to aid in careful selection of cases for examination.

Sweet[56] believes that the use of the peritoneoscope does not assist in the determination of the resectability of a local growth in the cardia or fundus of the stomach. In many such cases the tumor cannot be visualized by this means, but when liver involvement or abdominal carcinomatosis is suspected, peritoneoscopy should be carried out so as to avoid performing a major exploration in inoperable cases.

From a study of primary tumor of the liver, Warvi[109] concludes that biopsy is imperative. Peritoneoscopy offers some opportunity to determine operability in addition to obtaining a specimen for microscopic study. Resection of primary tumors of the liver may be indicated in adenomas, cystadenomas, localized solitary carcinomas and hemangiomas, with certain restrictions.

In a recent Cabot case record of the Massachusetts General Hospital[110] the value of peritoneoscopy in acute pancreatitis was demonstrated. During the peritoneoscopy the entire peritoneum, anterior gastric wall, small bowel and liver were seen to be covered with small, pale-yellowish implants averaging 2 mm. in diameter. Biopsy of one of these implants showed fat necrosis.

Volwiler[111] believes that under certain conditions in diffuse disease of the liver, aspiration biopsy[112] has proved highly satisfactory in diagnosis. When properly used it is easier than peritoneoscopy, but of course the site of selection of the tissue cannot be determined under direct vision. It has the advantage of being a simpler procedure than peritoneoscopy and also of securing a biopsy specimen from deep in the parenchyma of the liver. When carcinoma is suspected, a direct inspection should be made by peritoneoscopy.

Decker and Cherry[113] have found culdoscopy, or the endoscopic visualization of the pelvic organs by the vaginal route, superior to peritoneoscopy in the diagnosis of pelvic disease and in physiologic study. They believe that the procedure is invaluable in the investigation of pelvic tumors, ovarian disease, endometriosis and ectopic pregnancy and is especially helpful in the detailed study of primary and secondary sterility in women.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32281

PRESENTATION OF CASE

A fifty-nine-year-old Italian woman entered the hospital because of weakness and pain in both arms.

She was apparently well until twenty months before admission, when she had a pelvic operation the exact nature of which was not known, but which was done per vaginam and was apparently a repair of a cystocele. This operation was performed because of a burning sensation on urination. Two months later she developed pain in the left thigh and weakness of the legs, which tended to buckle under her when she climbed stairs. Ten months before entry the pain disappeared, but she noticed ankle swelling that gradually progressed up her legs. The weakness of the legs also progressed, and three months later she could no longer negotiate stairs without help and there was swelling up to the thighs. Two months later, she was seen at another hospital, where an x-ray examination of the chest, a gastrointestinal series, a barium enema, an intravenous pyelogram and peritoneoscopy were reported as negative. During her three-week stay in that hospital, the swelling of the legs decreased and continued to do so on a low-salt diet. She was discharged with a diagnosis of thrombophlebitis. Shortly afterward she began to have sharp pains in the calves and ankles that later progressed up to her hips, back and arms. She obtained some relief with heat and aspirin. At about the same time, she noted the onset of intermittent fever as high as 102°F., with such excessive sweating as to necessitate changing her bedclothes two or three times a night. She also had marked tremors in both hands. One month before entry the patient developed nocturia (three times) and also became anorexic. Her condition remained essentially unchanged until seven days before entry, when there was a sudden onset of pain in the arms, especially at the shoulders, elbows and wrists and in the neck, jaw and back of the head. Concomitantly she noticed marked weakness in both arms. During the year before admission she had lost about 25 pounds.

Her past history was noncontributory. She had borne eight children.

Physical examination revealed an ill appearing woman who did not move her arms, was perspiring freely and was apparently in pain. The left pupil was larger than the right, but both reacted normally to light. A firm, nontender, 3-cm. node was felt in the left axilla. There were dullness and absence of breath sounds at the right base. The liver edge was palpated three fingerbreadths below the costal margin, and a questionable mass was palpated below it. The vagina appeared constricted. No cervix or fundus could be felt. Examination of the arms revealed wasting of the deltoid and biceps muscles and absence of biceps and radial reflexes. The legs showed wasting of the quadriceps muscles, loss of knee and ankle jerks and moderate ankle edema. The only sensory changes were tenderness over the seventh cervical vertebra and over the anterior portion of the left mandible, with anesthesia of the left side of the chin, including the lower lip.

The temperature was 100°F., the pulse 120, and the respirations 24. The blood pressure was 155 systolic, 85 diastolic.

Examination of the blood showed a red-cell count of 4,200,000, a hemoglobin of 10.5 gm. and a white-cell count of 7300, with 74 per cent neutrophils and no abnormal cells. Another observer noted the presence of occasional nucleated red cells. The serum phosphorus was 4.3 mg. per 100 cc., and the alkaline phosphatase 5.3 Bodansky units. The nonprotein nitrogen was 24 mg. and the total protein 7.0 gm. per 100 cc., with an albumin-globulin ratio of 1.3. The cephalin flocculation test was negative after twenty-four hours and ± after forty-eight hours. A catheterized specimen of urine gave a ++++ test for albumin, and the sediment contained up to 20 white cells per high-power field. The specific gravity of four specimens ranged from 1.012 to 1.022. Two stool specimens were formed, brown and guaiac negative. The spinal fluid was negative except for a protein of 125 mg. and a sugar of 120 mg. per 100 cc., and 1000 red cells per cubic millimeter.

X-ray examination revealed areas of increased density in the right lower chest, probably involving the middle and lower lobes and consistent with collapse (Fig. 1). A small amount of fluid appeared to be present in the right pleural cavity. A plain film of the abdomen showed fixation of the right half of the diaphragm. It was not definite whether the area of density on the right side was above or below the diaphragm.

Despite supportive therapy the patient rapidly failed, becoming increasingly dyspneic and weak. She had constant diaphoresis. Thoracentesis was attempted between the sixth and seventh ribs posteriorly, but no fluid was obtained.

The patient died on the tenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED O. LUDWIG: I should like to begin by looking at the x-ray films.

DR. JAMES R. LINGLEY: These films show the marked elevation of the right half of the diaphragm, with density in the lower lung field that is consistent with collapse of the lower lobe. There is probably a small amount of fluid in the costophrenic angle. The plain film of the abdomen shows a moderate amount of gas in the colon. There is a shadow beneath the lower border of the liver that could be a gallstone or calcification in a costal cartilage.

DR. LUDWIG: Is that not a process in the lung?

DR. LINGLEY: I believe that there is collapse of the lower lobe. The diaphragm is elevated, and the elevation could be due to subdiaphragmatic disease or to collapse of the lung. The films do not help much on that. We also have a film of the cervical spine, which is negative.

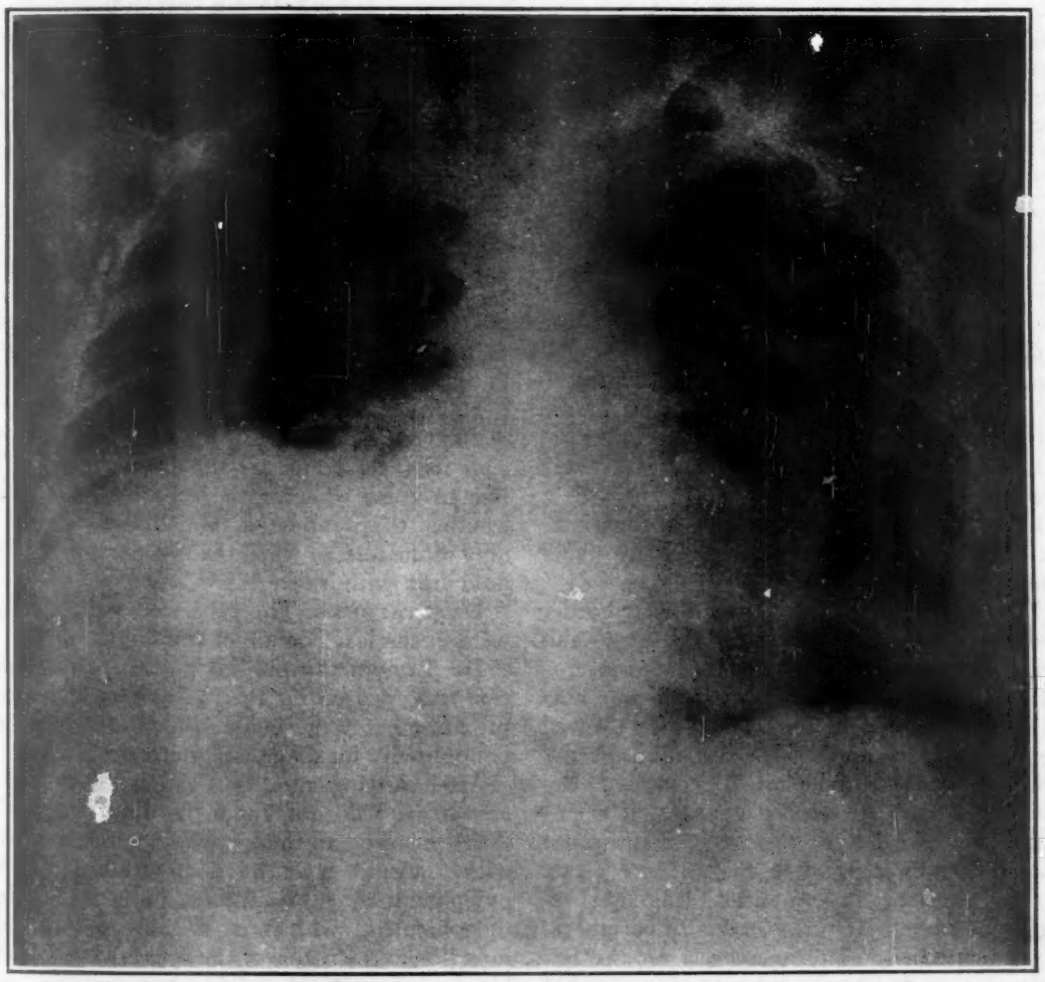

FIGURE 1.

DR. LUDWIG: It seems to me that the outstanding episode in this woman's illness is the development of pain and increasing weakness of the legs two months before entry, associated at first with rather marked edema. She was studied extensively elsewhere; we do not know what was found, but the diagnosis of thrombophlebitis was made. I do not see how anyone can say whether that was the correct diagnosis. It could have caused the symptoms that she presented. It is surprising that a swelling of the legs, supposedly due to circulatory obstruction, decreased on a low-salt diet. The next striking factor in this history is the onset of pains in the calves and ankles, with progression up to the hips. It is my impression that the pains were of neurologic rather than local origin. We know nothing about the condition of the joints at that time, and I think that we must assume that they were normal. About then she developed fever, which continued until the time of death. It is necessary to explain the origin of that fever. The first thing to think of is infection, since this woman had a deep-seated thrombophlebitis. I also think of cancer, of which there are no clues, however. Cancer could also account for the fever. In that regard lymphoma should certainly be considered. The tremors I cannot explain, although they may have been due to weakness. There is no indication that this woman had any

acute cerebral accident. The final and important part of the history is the sudden onset of pain in the arms, back of the head, various joints and jaw. I should be interested to know exactly what the joints looked like.

DR. JOHN STANBURY: The joints were normal.

DR. LUDWIG: I assumed that they were. Furthermore, arthritis or rheumatic fever could hardly have produced the picture described.

The patient had nocturia, from which I judge that some renal insufficiency was present. The history of anorexia and weight loss does not help much. They are consistent with any chronic illness, whether due to cancer or to chronic infection. The irregularity or the disproportion of the size of the pupils is not helpful to me, because there were no other pupillary abnormalities. I should like to know, of course, what that firm, nontender 3-cm. node in the left axilla was. It seems a little large to be accepted as a normal lymph node. The chest signs were not discussed by the roentgenologist, but he raised the question whether the trouble was above or below the diaphragm. Judging by later statements in this history, one must certainly consider something above the diaphragm because of the marked dyspnea that developed. The fact that the liver edge was three fingerbreadths below the costal margin is an important finding, as is the questionable mass palpated below it. I forgot to ask Dr. Lingley if he could see that mass in the x-ray film.

DR. LINGLEY: I do not see any mass. I think that the liver is enlarged.

DR. LUDWIG: Is the enlargement an intrinsic increase in size, or is the liver depressed by something above it?

DR. LINGLEY: You can see the lower border fairly well from the splenic flexure of the colon, and the entire liver shadow looks rather large to me.

DR. LUDWIG: The vaginal examination was normal. The examination of the arms which showed wasting of the muscles and the absence of biceps and radial reflexes, must also be taken seriously. Because of the absence of sensory changes, it seems to me that there must have been some disturbance in the anterior-horn cells or in the anterior roots. Without any sensory abnormalities, I do not see how one can assume that this was due to peripheral neuritis or neuronitis. The anesthesia on the left side of the chin, including the lower lip, is somewhat difficult to explain, and I believe that it was on the basis of some local interference of the roots of the fifth nerve going to that part of the face. I think that the other important finding in the physical examination is the tenderness over the upper cervical vertebras. The wasting of the quadriceps muscle and the loss of knee and ankle jerks probably mean the same thing in the lower extremities as in the upper extremities, namely, that there was some interference in the anterior-horn cells or roots.

The laboratory findings, so far as the blood is concerned, help me little. There was a moderate degree of secondary anemia. The serum phosphorus, the serum phosphatase and the total protein were within normal limits. I am not disturbed by the cephalin flocculation test. The ++++ test for albumin was found in a catheterized specimen, and if it is to be taken seriously, it indicates some type of renal disease. Four urine specimens had specific gravities ranging from 1.012 to 1.022. That means that she was still able to concentrate urine relatively well. Nevertheless the albuminuria is indicative of renal disease. The spinal-fluid findings are quite disturbing. Certainly the protein was markedly elevated, the normal upper range being somewhere around 45 mg. per 100 cc. The sugar value was high, since the normal spinal-fluid sugar ranges from 60 to 70 mg. per 100 cc. I should like to know what the blood sugar was. Incidentally, I cannot think of any neurologic condition that is characterized by an increase in the spinal-fluid sugar. Usually such an elevation mirrors a concomitant elevation of the blood sugar. Is there a record of the blood sugar?

DR. TRACY B. MALLORY: No blood sugar was recorded.

DR. LUDWIG: We shall have to throw out the finding of high sugar in the spinal fluid; I do not know what it means.

I think that we can say definitely that the finding of 1000 red cells per cubic millimeter was not responsible for the 125 mg. per 100 cc. of protein. I should like to know whether the cells were crenated, and whether they appeared immediately at the beginning of the test, or when the last portion of the spinal fluid was withdrawn.

DR. STANBURY: The cells were not crenated and were in the last portion of the fluid.

DR. LUDWIG: In the last phase of this case attention was focused on the right chest and unsuccessful attempts were made to withdraw some fluid, undoubtedly for diagnostic purposes.

After putting all this together, the most honest answer is, I do not know the diagnosis. I believe that the woman had thrombophlebitis to begin with. Could that have progressed to produce pylephlebitis? Certainly there is no evidence of pylephlebitis, which is usually associated with infection in the region of the appendix and is followed by an intermittent spiking temperature, multiple abscesses of the liver and jaundice, which usually runs a rapid course unless the infection is curtailed. It is possible that there was an infection in the region of the liver. If that were so, one of my guesses would be that there was a subdiaphragmatic abscess. I cannot say, however, that there is much evidence of such an abscess. Could this patient's symptoms be explained on the basis of multiple venous thromboses? I think that that is possible. There is nothing to suggest that the difficulty in the lung was

due to a pulmonary embolus: there was no hemoptysis or history of chest pains, and no indication of endocarditis or cardiac valvular disease. Finally how can one explain what happened in the spinal canal? The patient could have had a thrombosis or embolus in the spinal canal. It would be extremely unlikely for either condition not to produce a definite myelitis, with a level and with sensory changes that were not present in this case. I have seen one case in this hospital in which there was a high spinal-fluid protein without block, which was due to a hemangioma. I gather that there was no block in the case under discussion. Hemangiomas of the spinal cord, which occur on the posterior surface of the cord, usually produce fairly marked sensory changes. Another possibility is an epidural abscess in the bony structures in the area of the seventh cervical vertebra, with some encroachment on the spinal cord. Whatever happened there apparently happened suddenly. Whether a small abscess rapidly increased in size, or burst or produced some local thrombosis, I do not know. In either event an abscess in the region of the seventh cervical vertebra was probably found. Again, I am quite at a loss to explain the terminal episode in this woman's illness. We are told that she failed rather rapidly, showed increasing dyspnea, and died. This may represent a terminal pneumonic infection, but from what we are given I can draw no conclusion. I do not know why she died.

In summary, although I do not believe that I am close to the diagnosis, I think that this woman had a chronic infection. It is possible that she had multiple septic venous thrombosis or multiple abscesses — one in the region of her liver, followed by a subdiaphragmatic abscess, and another in the region of the seventh cervical vertebra. Cancer is always possible, and cannot be ruled out in this case. If a biopsy on the axillary lymph nodes had been done, much light would have been shed on this case.

DR. MALLORY: I think that you should have some additional information, Dr. Ludwig.

DR. LUDWIG: I do too.

DR. MALLORY: A biopsy of the axillary lymph node was made, but the answer was not available at the time the patient died.

A PHYSICIAN: Was a test for Bence–Jones protein done on the urine?

ANOTHER PHYSICIAN: The urine was examined for Bence–Jones protein and was negative.

CLINICAL DIAGNOSIS

Malignant lymphoma.

DR. LUDWIG'S DIAGNOSIS

Multiple septic thrombophlebitis, with secondary abscess formation (in region of liver and epidurally in cervical region)?
Malignant tumor (origin and type unknown)?

ANATOMICAL DIAGNOSES

Malignant lymphoma involving retroperitoneal tissues and meninges of spinal cord.
Thrombosis of right hepatic vein.
Thrombophlebitis of iliac vein, old.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Our first opinion in the laboratory was that the lymph node removed showed simple hyperplasia. On reconsideration we eventually decided that the diagnosis was giant follicular lymphoma. Autopsy showed an extensive retroperitoneal lymphoma involving the mesentery and the tissues around both kidneys. Histologically this also proved to be lymphomatous but showed no traces of follicle formation. The elevation of the diaphragm on the right must have been largely due to tumor around the right kidney. The liver was enlarged, not because of the few small foci of tumor but because of a thrombosis of the right hepatic vein, with a partial infarction of the entire right lobe of the liver. The spinal cord seemed at first negative, but on more careful examination the meninges were found to be focally infiltrated with tumor. This process was most marked in the region of the cauda, which seemed to account adequately for the weakness of the legs. There was some infiltration in the cervical region, but it hardly seemed enough to explain the severe pains in the arms, neck and head or their sudden development. I think that nerve roots must have been caught in the tumor infiltration at some point that we failed to discover. There was evidence of old thrombophlebitis in the iliac vein.

CASE 32282

PRESENTATION OF CASE

A fifty-year-old chauffeur entered the hospital because of epigastric pain.

The patient was apparently well until a week before admission, when he had an attack of evening "indigestion" accompanied by severe, dull, gnawing, nonradiating epigastric pain ("as if the stomach were twisting"), a feeling of pressure and a great deal of belching. He called his doctor, and was given morphine. The next day the symptoms had ceased. Two nights before entry, he had a similar episode and again received morphine. The night before admission there was a third recurrence of pain, which persisted until the following day despite two injections of morphine. He had no fever, chills, vomiting or nausea. His last bowel movement was one day before entry. His appetite was good until the present illness. There was no previous history of gastric distress, but he had always avoided fried foods and gravy. Six years before entry, the patient had an episode of weakness, at which time an electro-

cardiogram was reported as normal. There was no history of recent weight loss.

Physical examination revealed a drowsy man with constricted pupils who was still suffering from epigastric distress. The pupils responded to light. The tongue was dry and coated with a yellow film. The heart and lungs were normal. The abdomen was somewhat tense but not tender. No masses were felt.

The blood pressure was 130 systolic, 85 diastolic. The temperature was 99.5°F., the pulse 90, and the respirations 20.

Examination of the blood revealed a hemoglobin of 16.1 gm. and a white-cell count of 17,400, with 85 per cent neutrophils. The urine was negative except for a + test for albumin.

A plain film of the abdomen revealed a moderate quantity of gas and fecal material in the colon. In the right midabdomen there was a gas-filled loop of small bowel, which was not dilated. There were calcified lymph nodes just to the right of the lumbar spine. Two ring shadows were seen in the gall-bladder region. When the patient assumed the upright position one of these shadows dropped to the fundus, but the other remained in the region of the cystic duct.

At 2:00 p.m. on the day of admission, the patient was free of pain but still moderately under the influence of morphine. There was minimal residual tenderness over the area of the gall bladder. At 5:00 p.m. there was a recurrence of pain, subjectively located in the upper epigastrium. On palpation the right upper quadrant was much more rigid than the left. Sharp pain was elicited on palpation in the right upper quadrant just lateral to the border of the rectus muscle, and one observer felt a suggestion of a soft mass in that area. Morphine was again administered. By evening the abdominal spasm was limited to this rather sharply defined zone along the right costal margin, where another observer thought that he could feel a mass. The patient felt fairly well, but the temperature had risen to 102°F. and the white-cell count to 21,050.

On the second hospital day an operation was performed.

Differential Diagnosis

Dr. Claude E. Welch: In essence, this is the history of a fifty-year-old man with repeated attacks of severe epigastric pain that occurred within a week. The discussion of the differential diagnosis may be quickly limited to the gall bladder, pancreas, stomach and duodenum. In other words, was this an acute gall-bladder condition, acute pancreatitis or a perforated peptic ulcer?

The history eliminates the least likely diagnosis, perforated peptic ulcer. The patient had attacks of severe pain at intervals, but between them he was apparently free of distress. This is not the history of perforated ulcer. No mention is made of a plain film of the abdomen taken with the patient in a sitting posture, probably because the surgeon in charge did not consider perforated ulcer a possible diagnosis.

There is also little in the history to support the diagnosis of pancreatitis, which is usually ushered in by an acute attack of pain that is not remittent. Severe pancreatitis is frequently associated with vomiting. In the later stages, the white-cell count becomes high, although the temperature is likely to remain nearly normal. A blood amylase determination would have been of value so far as this diagnosis is concerned, but none is reported in the record.

One therefore returns to the most probable diagnosis — gall-bladder disease. So far as the exact type of disease is concerned, the intense pain, consisting of repeated steady attacks without nausea and without either chills or jaundice, indicates that there was no common-duct involvement and that the obstruction was in the cystic duct. Additional evidence is supplied by the x-ray film, which shows shadows of stone too large to pass through the cystic duct.

The rapidly rising temperature and the rising white-cell count under bed rest in the hospital suggest that a simple acute cholecystitis progressed to empyema. With this deterioration of the patient's condition operation was obviously indicated at an early stage, because of the impending danger of perforation.

There is no unequivocal evidence whether the gall bladder perforated. With a simple empyema of the gall bladder, a mass should have been easily palpable in a patient of normal size; there is nothing in the history to indicate that this patient was obese. Certainly the gall bladder was large when the x-ray film was taken, since one of the stones changed position.

I therefore believe that the gall bladder perforated after the x-ray film was taken and before the operation was performed. My final diagnosis is acute cholecystitis, with gangrene and perforation of the gall bladder and pericholecystic abscess.

Dr. Marshall K. Bartlett: When this patient was seen before operation, our line of reasoning was much the same as that of Dr. Welch. The patient had been so heavily medicated before admission that it was difficult to evaluate the exact status of the process, and it was decided to observe him overnight. By the next day it was obvious that the disease was progressing, and operation was deemed advisable. I did not feel a definite mass at any time.

Clinical Diagnoses

Acute cholecystitis.
Cholelithiasis.

Dr. Welch's Diagnoses

Acute cholecystitis, with gangrene and perforation of gall bladder and pericholecystic abscess.
Cholelithiasis.

Anatomical Diagnoses

Acute and chronic cholecystitis.
Cholelithiasis.

Pathological Discussion

Dr. Bartlett: At operation, thirty-six hours after the onset of the attack, there were a few fresh adhesions to the gall bladder, which was tense, edematous and obviously acutely inflamed. It contained several large stones. The cystic duct was small. Nothing abnormal was felt in the common duct, which was therefore not explored. The cystic duct and artery were isolated and tied. The gall bladder was removed in the usual manner without particular difficulty. The patient made an uneventful recovery, and was discharged on the eleventh day after operation.

Dr. Benjamin Castleman: The gall bladder that we received in the laboratory was edematous and porky and measured 7 mm. in thickness. A large patch of fibrinous exudate was present on the serosal surface, and the mucosa was markedly hemorrhagic and necrotic. There was therefore evidence of both acute and chronic inflammation.

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The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

HOSPITALS FACE CRITICAL SITUATION

Most of the hospitals in the Boston area are experiencing great difficulty in getting enough people to care for their patients. This includes graduate nurses, licensed attendants, ward helpers and ward maids.

The salaries of all these groups of people have been advanced to meet the increased cost of living. When all is said and done, the salaries of nurses compare favorably with those paid in government hospitals when it is realized that nurses working in civilian hospitals can choose their place of occupation.

There is no question that there is a shortage of nurses. No one knows just why: whether it is because so many nurses are getting married; whether so many nurses are accepting their privileges under the G. I. Bill of Rights; whether so many nurses are engaged in private duty; or whether so many nurses are entering service in the hospitals of the Army, Navy, Veterans Administration and Public Health Service. One cannot help wondering whether nurses realize the full seriousness of the situation in relation to the public's health.

The Massachusetts General Hospital had to close 80 of its beds in May, although a few of these were reopened in June. The Massachusetts Eye and Ear Infirmary is facing a serious shortage of nurses and has had to close its children's ward and nursery; emergency children's cases, however, are admitted and cared for in a section of the adult ward.

Hospital trustees, administrators, institutional nurses and employees have done and are doing everything that they can think of to remedy this situation. Little more can be done other than to let everyone, including patients, potential patients, possible employees, physicians, nurses and others, know what the situation is. The matter has now become a community as well as a hospital problem.

LIFE INSURANCE MEDICAL RESEARCH FUND STARTS SECOND YEAR

It is generally agreed that fundamental research in science is useful and deserving of support. It is also well known that such research has become increasingly expensive and that the funds available for that purpose have not kept pace with the growing needs. Because the prospects of sustaining and expanding research in the physical and biologic sciences by private funds are steadily diminishing, new sources for support of activities in these fields have been sought. The many useful results achieved by governmental support of scientific research connected with the war effort have stimulated activity in favor of inaugurating a system whereby the physical and biologic sciences and scientists in these fields could receive appropriate aid from governmental funds. Most scientists, however, suspect that such support implies political dictation and control, as well as an unnecessary amount of red tape. They therefore prefer other sources of funds, if they

can be provided. Those who hold that opinion believe that all possible private sources should be explored and that these agencies should be encouraged to provide the necessary funds, free of all encumbrances.

With respect to research in the medical sciences, its primary and long range purpose, broadly speaking, is to keep the greatest number of people in the best of health for the longest time. That purpose coincides exactly with the objectives of all life-insurance companies. To them the accomplishment of this purpose means increasing returns in terms of dollars and cents. It is therefore not surprising that executives of the majority of the large life-insurance companies in the United States and some in Canada have pooled funds for the support of basic research in medical problems and have entrusted these funds to an organization called the Life Insurance Medical Research Fund. The advisory council of this fund includes a group of medical investigators from different universities, most of whom have had considerable experience with the administration of research funds.

The first annual report of the Life Insurance Medical Research Fund, that for the year 1945, has recently been mailed to the one hundred and forty-eight sponsoring companies in the United States and Canada. During that time $126,525 was earmarked for grants already approved for eight research projects underway at six medical schools. Because of conditions associated with the termination of the war, only 25 per cent of the annual contributions of the various member companies was called for in 1945, but it is the intention of the fund to call for full contributions, amounting to approximately $580,000, in 1946. The chairman of the Board of Directors of the Fund states that the program holds much promise of good for both policyholders and the general public. The type of research that is being supported is fundamental in character and concerns, among other things, investigations into the basic causes of rheumatic fever, hypertension and arteriosclerosis. It is fully appreciated that tangible results in such researches must not be looked for too soon, and it is implied that the Fund will continue to support plans of research on a long-term basis.

There are many other private groups that would also benefit by developments along similar lines. Thus, the manufacturers of pharmaceuticals and industrialists in general have long-range interests in this field, and their promotion of fundamental research by the financial support of teachers and investigations in medical sciences could not fail to be a good investment. They should be encouraged to follow the lead of the life-insurance companies.

MASSACHUSETTS MEDICAL SOCIETY

SUBCOMMITTEE ON VETERANS' AFFAIRS, COMMITTEE ON POSTWAR PLANNING

The Subcommittee on Veterans' Affairs, composed of G. Philip Grabfield, chairman, Victor G. Balboni, George P. Denny, Alexander Marble and George F. Wilkins, has been enlarged to include representatives of all the district medical societies. The representatives thus far appointed are as follows:

Barnstable: Sheldon L. Hunt, Yarmouth Port
Berkshire: Franklin K. Paddock, Pittsfield
Bristol North: Leonard W. Hill, Attleboro
Bristol South: Merrill F. Gardner, Fairhaven
Essex North: Louis B. Simard, Haverhill
Essex South: Frank P. Morse, Jr., Salem
Franklin: Spencer C. Flo, Greenfield
Hampshire: Stephen Brown, Northampton
Middlesex East: William M. Gowen, Melrose
Middlesex North: Thomas J. G. Tighe, Lowell
Middlesex South: John C. McGirr, Belmont
Norfolk: Leo R. Desmond, Dorchester
Norfolk South: Ensio K. F. Ronka, Wollaston
Plymouth: William M. Carr, Whitman
Suffolk: Charles H. Bradford, Boston
Worcester: Thomas Hunter, Shrewsbury

Any veteran physician with problems or suggestions in relation to veterans' affairs should communicate with his district representative or the chairman.

G. PHILIP GRABFIELD, *Chairman*

MISCELLANY

PUBLIC-HEALTH CONFERENCE IN CHINA

News has been received from Lieutenant Colonel Merrill Moore, M.C., A.U.S., to the effect that he took an active part in the organization of the first public-health conference to be held in China during the past ten years. The conference was sponsored by Major General Robert B. McClure, commanding general of the Nanking Headquarters Command, United States Army Forces, and by General Ho Yin-Ching, supreme commander of the Chinese Army, and was held on Saturday, April 20, in the Assembly Hall of the Supreme Headquarters of the Chinese Army at Nanking. The program comprised sixteen addresses, the majority in Chinese, having to do with various aspects of preventive medicine and hygiene.

BOOKS RECEIVED

The receipt of the following book is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

What to Do about Vitamins. By Roger J. Williams, Ph.D., director of the Biochemical Institute, University of Texas. 8°, cloth, 56 pp. Norman, Oklahoma: University of Oklahoma Press, 1945. $1.00.

This popular manual discusses the necessity of vitamins and minerals in the diet and how they may be secured in adequate amounts. The text is illustrated with tables, graphs and charts for easy reference. Appended to the text is an interesting table of the vitamin content of the common foods, both vegetable and animal.

Total War and the Human Mind: A psychologist's experiences in occupied Holland. By A. M. Meerloo, M.D., F.R.S.M. 8°, cloth, 78 pp. New York: International Universities Press, Incorporated, 1945. $1.75.

In this book Dr. Meerloo has drawn on his experiences of two years in occupied Holland and discusses such themes as mass reaction to German occupation, Hitler's psychologic weapons, the psychology of radio propaganda and how the body is affected by fear.

Pharmaceutical Calculations. By Willis T. Bradley, A.M., and Carroll B. Gustafson, Ph.C., A.M. 8°, cloth, 283 pp. Philadelphia: Lea and Febiger, 1945. $2.75.

This manual is based on the *Pharmaceutical Arithmetic* of Professor Theodore J. Bradley but is substantially a new work, since it includes theoretical discussions and explanations preceding examples and practice deliberately excluded from the original work.

Much new material has been added, including a simplified equation for converting centigrade and Fahrenheit scales, a new approach to ratio and percentage and dilution problems consistent with the *Pharmacopoeia* and an original treatment of isotonic problems.

It includes careful definition of terms and is intensely practical in its application. Appendices contain related matter on problems in general chemistry, weights and volumes of gases, proof strength, emulsions, solubility ratios and tables of epitonic equivalents, dilution, weight and volume of water and atomic weights.

This small volume should prove of value not only to students and teachers of pharmacy but also to pharmacists, chemists, physicians, nurses and all others confronted with the problems of arithmetical problems in pharmacy. It is recommended for reference purposes to medical and allied libraries.

Lights Out. By Baynard Kendrick. 8°, cloth, 240 pp. New York: William Morrow and Company, 1945. $2.50.

This is the story of a blinded soldier and his conditioning in Army hospitals for a normal everyday life.

The Male Hormone. By Paul de Kruif. 8°, cloth, 243 pp. New York: Harcourt, Brace and Company, 1945. $2.50.

DeKruif, in another of his popular books on medical subjects, narrates the story of the long struggle to isolate the male hormone until its discovery by the chemists, Ruzicka and Butenandt, in 1935, who later were awarded the Nobel prize for their work. The author then relates in plain language the use of testosterone in revitalizing men suffering from poor health due to sexual insufficiency.

Your Hair and Its Care. By Oscar L. Levin, M.D., and Howard T. Behrman, M.D. 12°, cloth, 184 pp. New York: Emerson Books, Incorporated, 1945. $2.00.

The authors are dermatologists who have written in plain language an up-to-date popular manual on the human hair. They tell what to do to save and beautify the hair and to stimulate healthier growth and discuss such conditions as baldness of various types, dandruff, infections of the scalp, abnormal types of hair and the effects of occupations on the hair.

Moderne Eisentherapie. By Rudolf Stodtmeister and Peter Büchmann. With introductory remarks by Professor Dr. R. Siebeck, of Heidelberg, and Professor Dr. L. Heilmeyer, of Jena. 8°, cloth, 120 pp. Ann Arbor: J. W. Edwards, Incorporated, 1944. $3.75. Published and distributed in the Public Interest by Authority of the Alien Property Custodian under License No. A-492.

This monograph in German has been considered of sufficient importance to be reproduced by lithoprinting from the original Stuttgart edition of 1943. This fact alone speaks well for the importance of the work. About half the text discusses the use of iron in the treatment of the anemias, including the pernicious and aplastic types. The first two chapters have to do with the role of iron in the human organism and iron resorption. These are followed by a brief consideration of the general indication of iron in treatment and then by a section on the clinical use of iron in the anemias. The last short chapter is miscellaneous in character, discussing such topics as blood transfusion and iron therapy, iron and arsenic, iron preparations, length of treatment, intravenous use and liver treatment. The text is compact and in simple German. This monograph should be in all medical libraries and on the shelves of all physicians specializing in blood diseases.

NOTICES

ANNOUNCEMENTS

Dr. R. H. Aldrich announces the removal of his office to 422 Beacon Street, Boston.

Dr. Nathaniel Bennett, having returned from military service, announces the opening of an office at 646 Sumner Avenue, Springfield.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, July 18

Friday, July 19

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

Tuesday, July 23

*12:00 m.–1:00 p.m. Dermatological Service, Grand Rounds. Amphitheater, Dowling Building, Boston City Hospital.

12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

Wednesday, July 24

*10:30–11:30 a.m. Medical Clinic. Isolation Building, Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:30–4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

March 15–September 15. Boston University Course for Discharged Medical Officers. Page 240, issue of February 14.

September 4–7. American Congress of Physical Medicine. Page 616, issue of May 2.

September 30–October 3. Industrial Health Congress. Page 878, issue of June 27.

October 6–12. Interamerican Congress of Cardiology. Page xix, issue of June 6.

October 7–18. New York Academy of Medicine. Page 544, issue of April 18.

February 7. American Board of Obstetrics and Gynecology. Page 34, issue of July 4.

District Medical Society

Plymouth

October. Jordan Hospital, Plymouth.
November. Plymouth County Hospital, South Hanson.
January. Brockton Hospital, Brockton.
February. Moore Hospital, Brockton.
March. Goddard Hospital, Brockton.
April. State Farm, Bridgewater.
May. Lakeville Sanatorium, Lakeville.